

Fig.1.

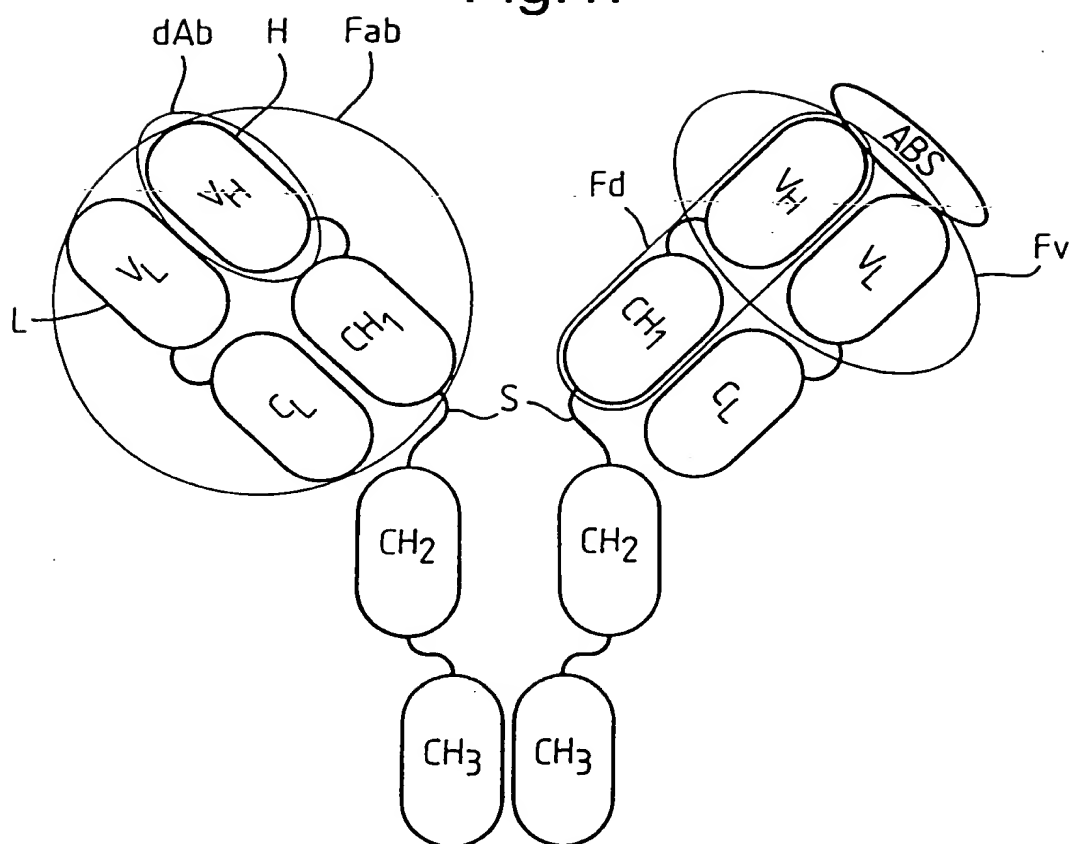


Fig. 2a

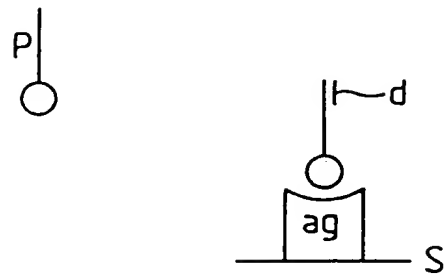


Fig. 2b

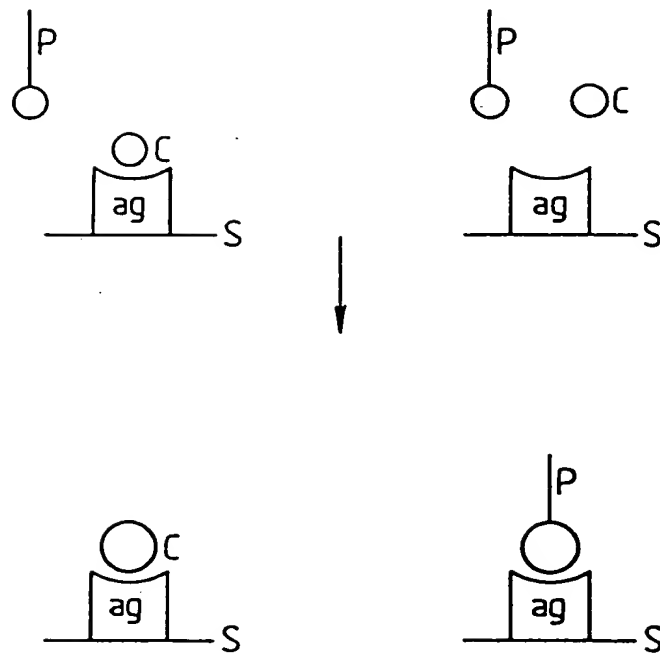


Fig.3.

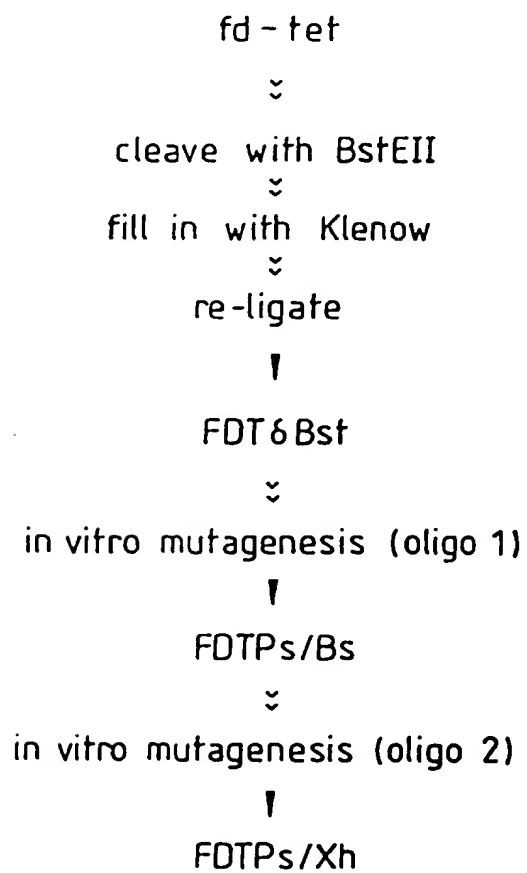
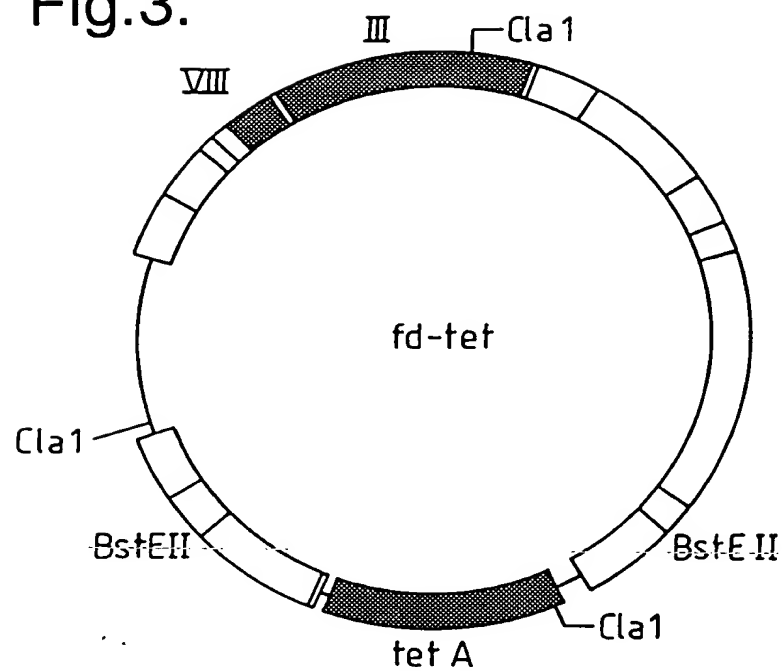


Fig. 4a

Fig. 4b

A TCT CAC TCC GCT

Fig. 5a

rbs M K Y L L P T A A
 GCATGCAAATTCCTATTTCAAGGAGACAGTCATAATGAAATACCTATTGCCTACGGCAGCC
 10 20 30 40 50 60
 SphI
 pelB leader
 A G L L L L A A O P A M A Q V Q L Q E S
 GCTGGATTGTTATTACTCGCTGCCCAACCAGCGATGGCCCAGGTGCAGCTGCAGGAGTCA
 70 80 90 100 110 120
 PstI
 G P G L V A P S Q S L S I T C T V S G F
 GGACCTGGCCTGGTGGCGCCCTCACAGAGCCTGTCCATCACATGCACCGTCTCAGGGTTC
 130 140 150 160 170 180
 S L T G Y G V N W V R Q P P G K G L E W
 TCATTAACCGGCTATGGTGTAAACTGGGTTCCGCGCCTCCAGGAAAGGGTCTGGAGTGG
 190 200 210 220 230 240
 VHD1.3
 L G M I W G D G N T D Y N S A L K S R L
 CTGGGAATGATTGTGGGGTGATGGAAACACAGACTATAATTCAGCTCTCAAATCCAGACTG
 250 260 270 280 290 300
 S I S K D N S K S Q V F L K M N S L H T
 AGCATCAGCAAGGACAACCTCCAAGAGCCAGTTTTCTTAAAAATGAACAGTCTGCACACT
 310 320 330 340 350 360
 D D T A R Y Y C A R E R D Y R L D Y W G
 GATGACACAGCCAGGTACTACTGTGCCAGAGAGAGAGATTATAGGCTTGACTACTGGGGC
 370 380 390 400 410 420
 Linker Peptide
 Q G T T V T V S S G G G G S G G G S G
 CAAGGCACCAACGGTCAACGCTCTCCTCAGgtggaggcggttcaggcgagggtggctctggc
 430 440 450 460 470 480
 BstEII
 G G G S D I E L T Q S P A S L S A S V G
 ggtggcggatcgGACATCGAGCTCACTCAGTCTCCAGCCTCCCTTTCTGCGTCTGTGGGA
 490 500 510 520 530 540
 SacI

Fig. 5b

E T V T I T C R A S G N I H N Y L A W Y
GAAACTGTCACCATCACATGTCGAGCAAGTGGGAATATTCACAATTATTTAGCATGGTAT
550 560 570 580 590 600

Q Q K Q G K S P Q L L V Y Y T T T L A D
CAGCAGAAACAGGGAAAATCTCCTCAGCTCCTGGTCTATTATACACAACCTTAGCAGAT
610 620 630 640 650 660

VKD1.3

G V P S R F S G S G S G T Q Y S L K I N
GGTGTGCCATCAAGGTTTCAGTGGCAGTGGATCAGGAACACAATATTCTCTCAAGATCAAC
670 680 690 700 710 720

S L Q P E D F G S Y Y C Q H F W S T P R
AGCCTGCAACCTGAAGATTTTGGGAGTTATTACTGTCAACATTTTGGAGTACTCCTCGG
730 740 750 760 770 780

Myc Tag (TAG1)

T F G G G T K L E I K R E O K L I S E E
ACGTTCCGGTGGAGGGACCAAGCTCGAGATCAAACGGGAACAAAACTCATCTCAGAAGAG
790 800 810 820 830 840

XhoI

D L N * * (SEQ ID NO. 183)

GATCTGAATTAATAATGATCAAACGGTAATAAGGATCCAGCTCGAATTC (SEQ ID NO. 184)
850 860 870 880

EcoRI

Fig.6.

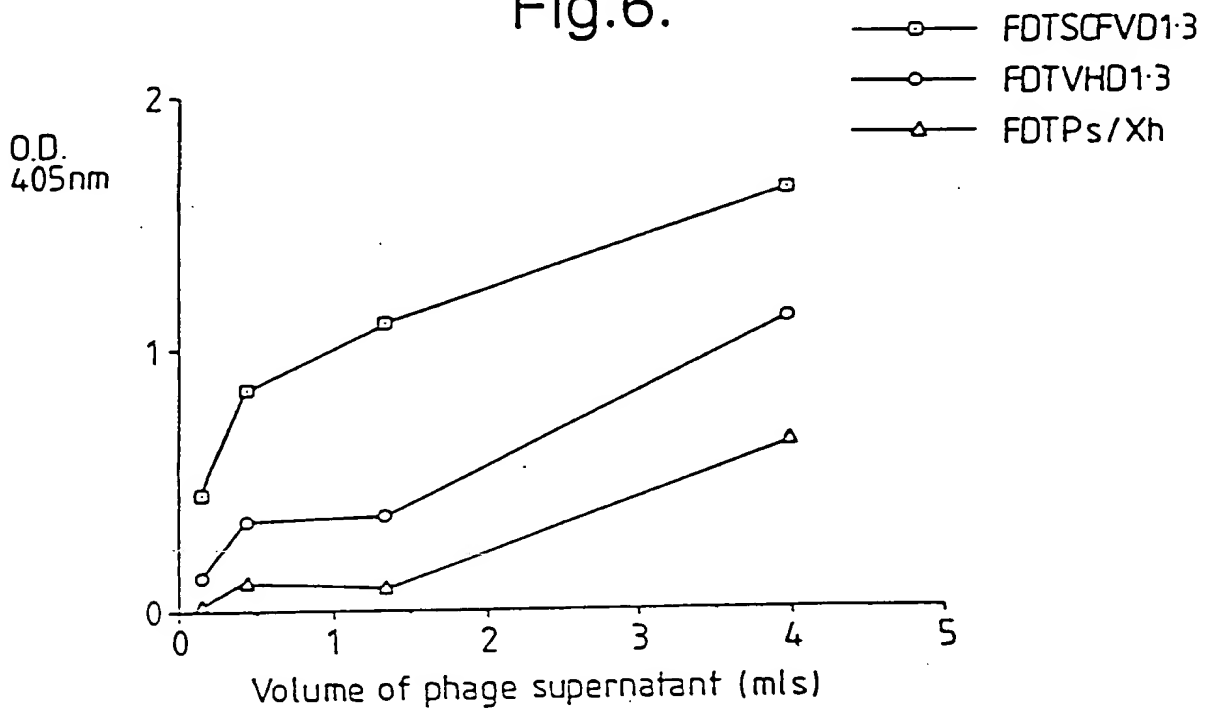


Fig.7.

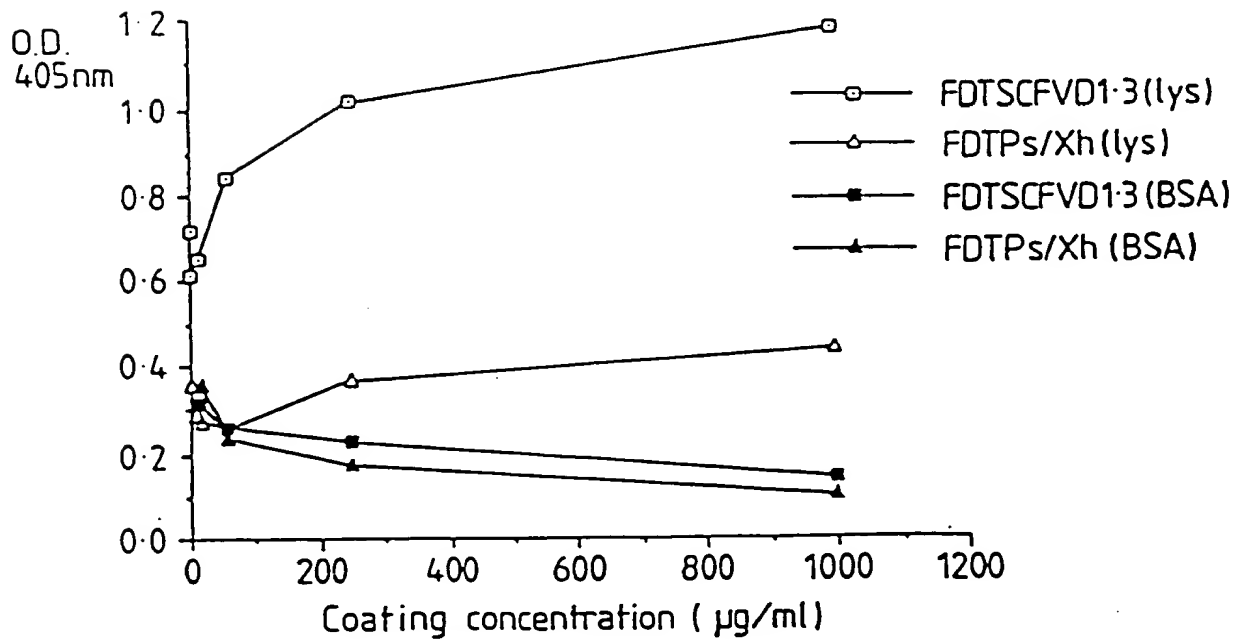


Fig.8.

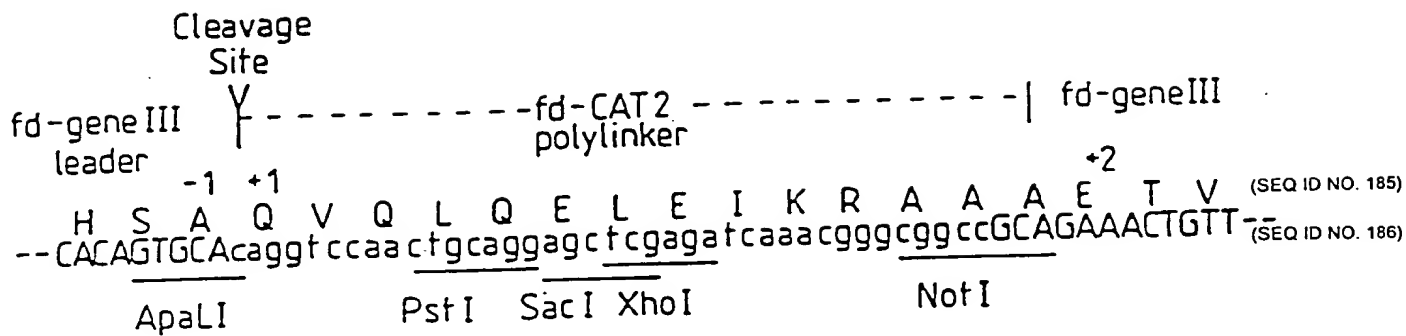


Fig.9.

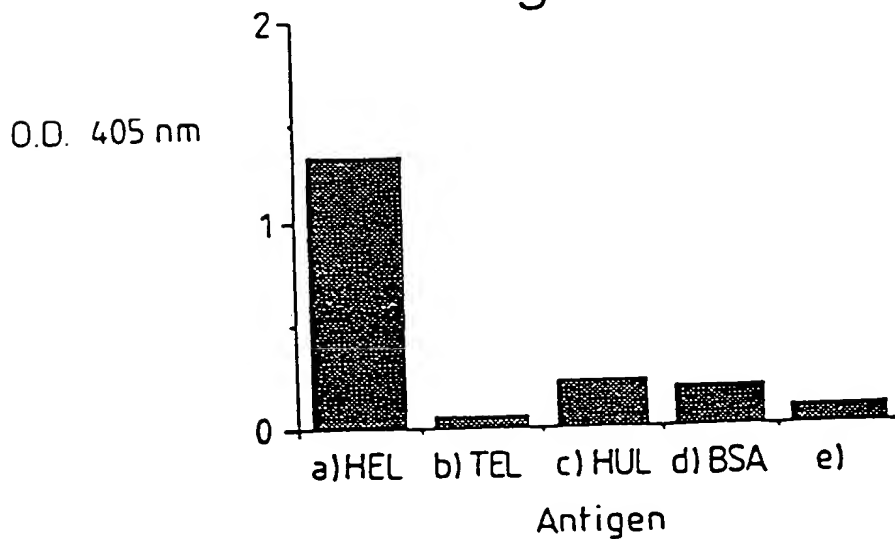


Fig. 10a

M K Y L L P T A A
GCATGCAAATTCTATTTCAGGAGACAGTCATAATGAAATACCTATTGCOCTACGGCAGCC
10 20 30 40 50 60

A G L L L L A A Q P A M A Q V Q L Q E S
GCTGGATTGTTATTACTGCTGCCCCAACCAGCGATGGCCCCAGGTGCAGCTGCAGGAGTCA
70 80 90 100 110 120

G P G L V A P S Q S L S I T C T V S G F
GGACCTGGCOCTGGTGGGGCCCCCTCACAGAGCOCTGTCCATCACATGCAACCGTCTCAGGGTTC
130 140 150 160 170 180

S L T G Y G V N W V R Q P P G K G L E W
TCATTAAACGGCTATGGTGTAAACTGGGGTTGCCCAGCOCTCCAGGAAGGGTCTGGAGTGG
190 200 210 220 230 240

L G M I W G D G N T D Y N S A L K S R L
CTGGGAATGATTTGGGGTGATGGAAACACAGACTATAATTTCAGCTCTCAAAATCCAGACTG
250 260 270 280 290 300

S I S K D N S K S Q V F L K M N S L H T
AGCATCAGCAAGGACAACCTCCAAGAGCCCAAGTTTCTTAAAAATGAACAGTCTGCACACT
310 320 330 340 350 360

D D T A R Y Y C A R E R D Y R L D Y W G
GATGACACAGCCAGGTACTACTGTGCCAGAGAGAGAGATTATAGGCTTGACTACTGGGGC
370 380 390 400 410 420

Q G T T V T V S S A S T K G P S V F P L
CAAGGCACCAAGGTCAACCGTCTCTCTCAGCOCTCCACCAAGGGCCCCATGGGTCTTCCCCCTG
430 440 450 460 470 480

A P S S K S T S G G T A A L G C L V K D
GCACCOCTCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGAC
490 500 510 520 530 540

Fig. 10b

Y F P E P V T V S W N S G A L T S G V H
TACTTCCCCGAAACCGGTGAACGGTGTCTGTGGAACTCAGGGGCCCTGACCCAGGGGGGTGCAC
550 560 570 580 590 600

T F P A V L Q S S G L Y S L S S V V T V
ACCTTCCCGGCTGTCTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGAACCGTG
610 620 630 640 650 660

P S S S L G T Q T Y I C N V N H K P S N
CCCTCCAGTAGCTTGGGCAACCAGACCTACATCTGCTAACGTGAATCACAAGCCCCAGCAAC
670 680 690 700 710 720

T K V D K K V E P K S S * * (SEQ ID NO. 187)
ACCAAGGTGACACAGAAAGTTCAGCCCAATCTTCATAATAACCCGGGAGCTTGCATGCA
730 740 750 760 770 780

M K Y L L P T A A A G L
AATTCTATTTCAGGAGACAGTCTATGAAATACCTATTGCCTACGGCAGCCGCTGGAT
790 800 810 820 830 840

L L L A A Q P A M A D I E L T Q S P A S
TGTTTATTACTGTGCTGCCCAACCAGCGATGGCCGACATCGAGCTCACCCAGTCTCCAGCCT
850 860 870 880 890 900

L S A S V G E T V T I T C R A S G N I H
CCCTTTCGTGCGTCTGTGGGAGAACTGTCAACCATCACATGTCTAGCAAGTGGGAATATTC
910 920 930 940 950 960

N Y L A W Y Q Q K Q G K S P Q L L V Y Y
ACAATTATTTAGCATGGTATCAGCAGAAACAGGCAAAATCTCTCTAGCTCCCTGGTCTATT
970 980 990 1000 1010 1020

Fig. 10c

T T T L A D G V P S R F S G S G S G T Q
ATACAACAACCTTAGCAGATGGTGTGCCATCAAGGTTCAGTGGCAGTGGATCAGGAACAC
1030 1040 1050 1060 1070 1080

Y S L K I N S L Q P E D F G S Y Y C Q H
AATATTCTCTCAAGATCAACAGCCTGCGCCTGAAGATTTTGGGAGTTATTACTGTCAAC
1090 1100 1110 1120 1130 1140

F W S T P R T F G G G T K L E I K R T V
ATTTTGGAGTACTCCTCGGACGTTGGGTGGAGGCACCAAGCTCGAGATCAAACGGACTG
1150 1160 1170 1180 1190 1200

A A P S V F I F P P S D E Q L K S G T A
TGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAAGT
1210 1220 1230 1240 1250 1260

S V V C L L N N F Y P R E A K V Q W K V
CCTCTGTTGTGTGCCGTGTAATAACTTCTATCCACAGAGGCCAAAGTACAGTGGGAAG
1270 1280 1290 1300 1310 1320

D N A L Q S G N S Q E S V T E Q D S K D
TGGATAACGCCCTCCCAATCGGGTAACTCCAGGAGAGTGTCAACAGACAGGACAGCAAGG
1330 1340 1350 1360 1370 1380

S T Y S L S S T L T L S K A D Y E K H K
ACAGCACCTACAGCCTCAGCAGCAACCTGACGCTGAGCAAAGCAGACTACGAGAAACACA
1390 1400 1410 1420 1430 1440

V Y A C E V T H Q G L S S P V T K S F N
AAGTCTACGCCCTGCGAAGTCAACCATCAGGGCCTGAGCTGCGCCGTCAAAAGAGCTTCA
1450 1460 1470 1480 1490 1500

R G E S * * (SEQ ID NO. 188)
ACCGGGGAGAGTCATAGTAAGAATTC (SEQ ID NO. 189)
1510 1520

Fig. 10d

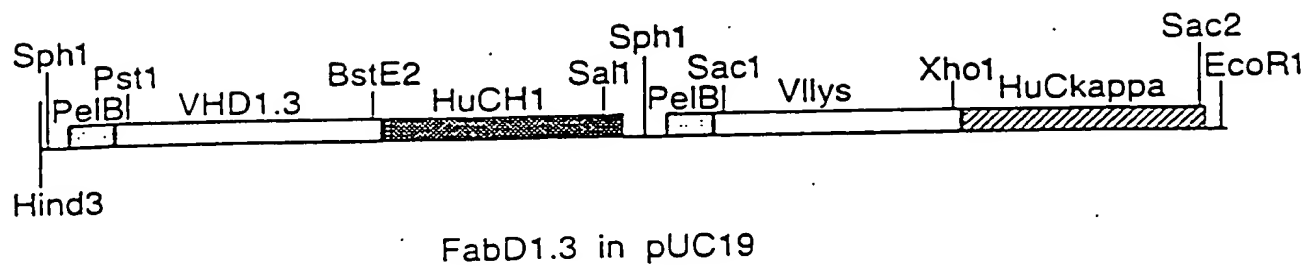


Fig.11.

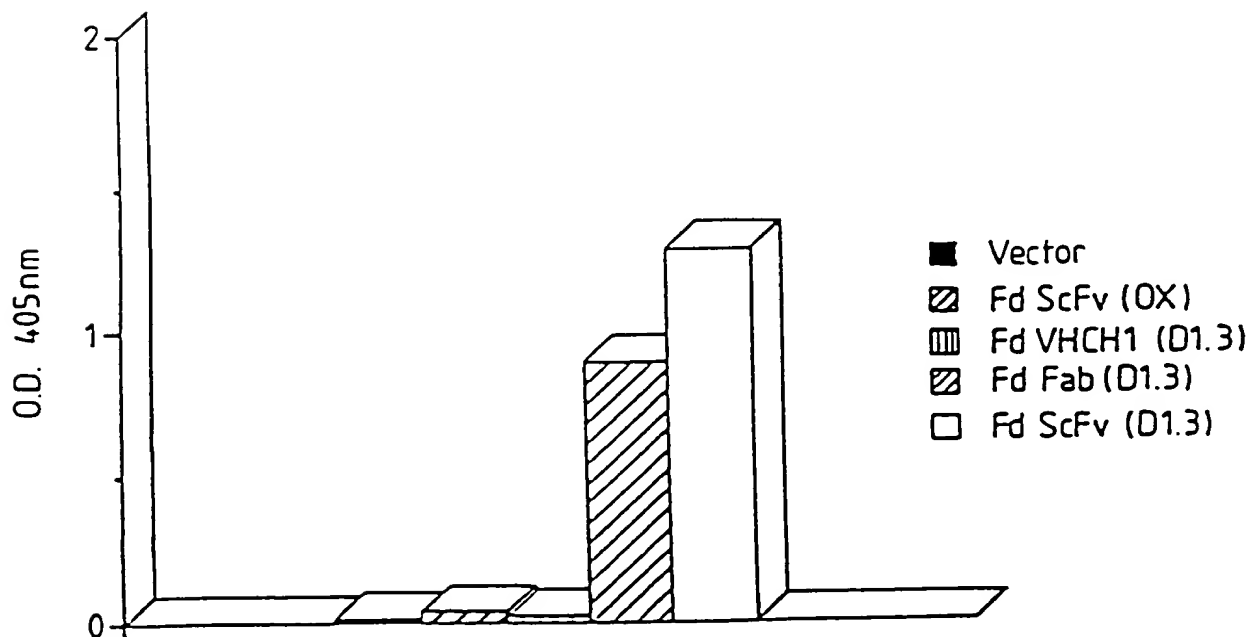


Fig.12a.

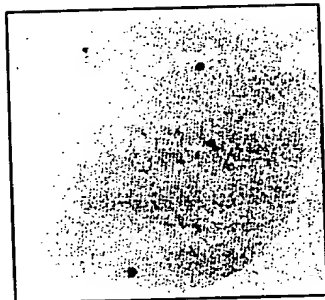


Fig.12b.

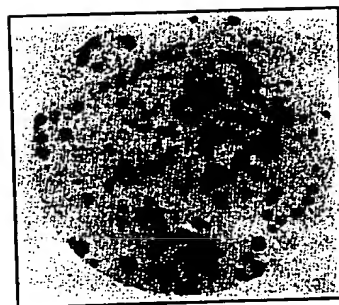


Fig.13.

Q V Q L Q E S G G G L V Q P G G
 CAG GTG CAG CTG CAG GAG TCA GGA GGA GGC TTG GTA CAG CCT GGG GGT
 PstI
 S L R L S C A T S G F T F S N Y
 TCT CTG AGA CTC TCC TGT GCA ACT TCT GGG TTC ACC TTC AGT AAT TAC
 Y M G W V R Q P P G K A L E W L
 TAC ATG GGC TGG GTC CGC CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG
 G S V R N K V N G Y T T E Y S A
 GGT TCT GTT AGA AAC AAA GTT AAT GGT TAC ACA ACA GAG TAC AGT GCA
 S V K G R F T I S R D N F Q S I
 TCT GTG AAG GGG CGG TTC ACC ATC TCC AGA GAT AAT TTC CAA AGC ATC
 L Y L Q I N T L R T E D S A T Y
 CTC TAT CTT CAA ATA AAC ACC CTG AGA ACT GAG GAC AGT GCC ACT TAT
 Y C A R G Y D Y G A W F A Y W G
 TAC TGT GCA AGA GGC TAT GAT TAC GGG GCC TGG TTT GCT TAC TGG GGC
 Q G T L V T v s s g g g g s g g g g s
 CAA GGG ACC CTG GTC ACC gtc tcc tca ggaggaggcggttcaggcggagggtggctct
 BstEII
 g g g g s d i E L T Q T P L S L P V
 ggcggtggcggtcggac atc GAG CTC ACC CAA ACT CCA CTC TCC CTG CCT GTC
 SacI
 S L G D Q A S I S C R S S Q S I
 AGT CTT GGA GAT CAA GCC TCC ATC TCT TGC AGA TCT AGT CAG AGC ATT
 V H S N G N T Y L E W Y L Q K P
 GTA CAT AGT AAT GGA AAC ACC TAT TTA GAA TGG TAC CTG CAG AAA CCA
 PstI
 G Q S P K L L I Y K V S N R F S
 GGC CAG TCT CCA AAG CTC CTG ATC TAC AAA GTT TCC AAC CGA TTT TCT
 G V P D R F S G S G S G T D F T
 GGG GTC CCA GAC AGG TTC AGT GGC AGT GGA TCG GGG ACA GAT TTC ACA
 L K I S R V E A E D L G V Y Y C
 CTC AAG ATC AGC AGA GTG GAG GCT GAG GAT CTG GGA GTT TAT TAC TGC
 F Q G S H V P Y T F G G G T K L
 TTT CAA GGT TCA CAT GTT CCG TAC ACG TTC GGA GGG GGG ACC AAG CTC
 E I K R
GAG ATC AAA CGG (SEQ ID NO. 190)
 XhoI (SEQ ID NO. 191)

Fig.14.

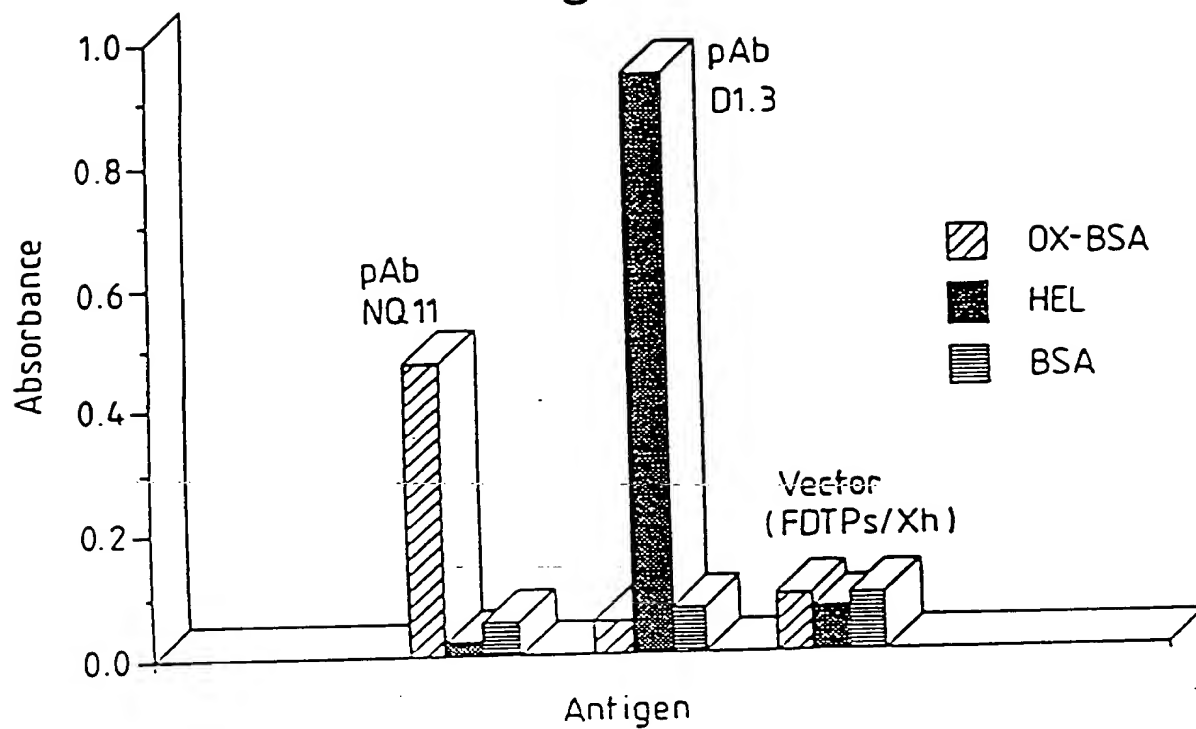


Fig.15.

5' END

TCT CAC AGT GCA CAA ACT GTT GAA CGG ACA CCA GAA ATG CCT GTT CTG (SEQ ID NO. 192)
 (SEQ ID NO. 193)
 ApaL1

3' END

K A A L G L K
 AAA GCC GCT CTG GGG CTG AAA GCG GCC GCA GAA ACT GTT GAA AGT etc.
 Not I

Fig. 16a

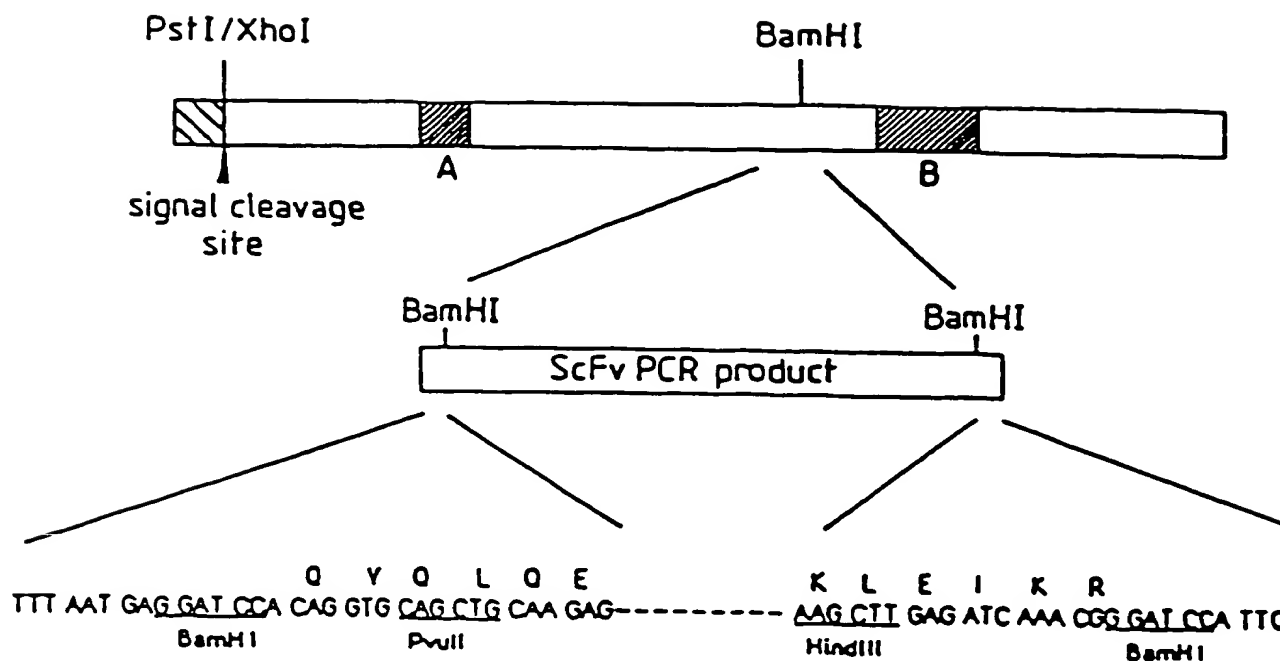
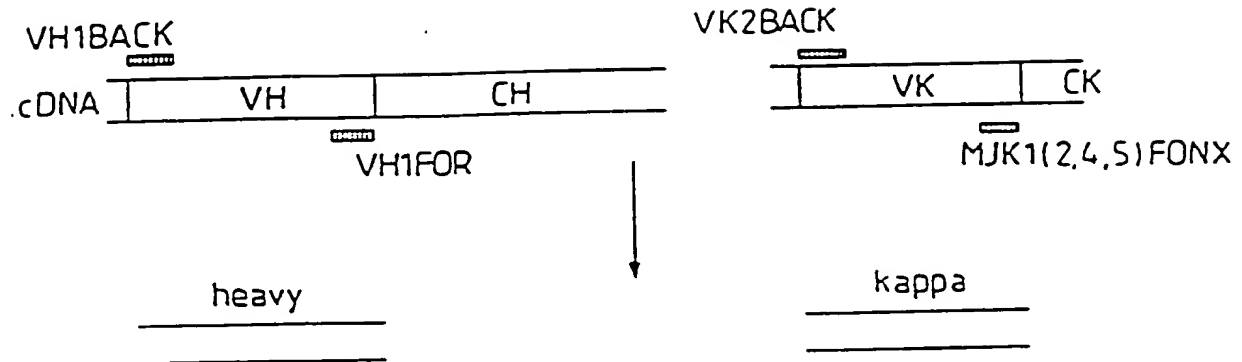


Fig. 16b

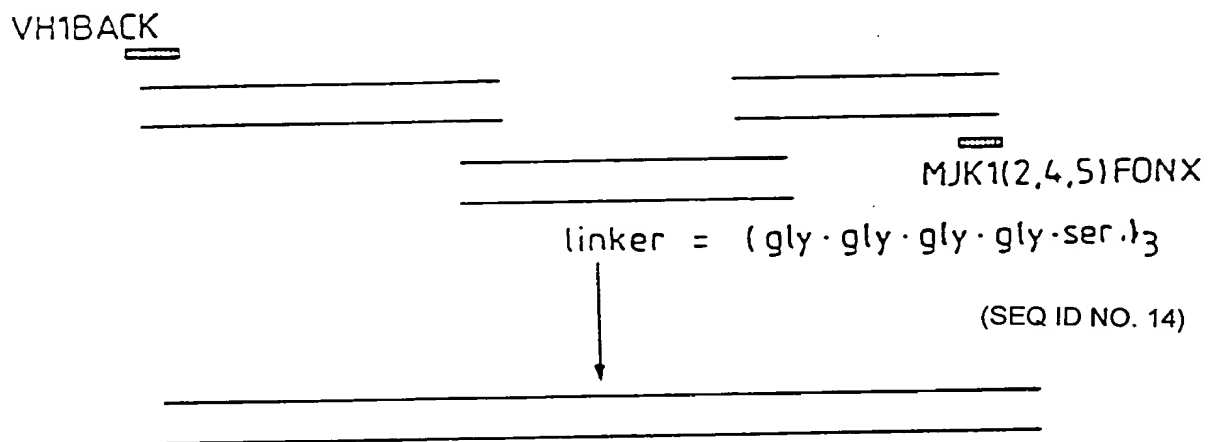
A	(1834) 5'	GAG GGT GGT GGC TCT	(SEQ ID NO. 200)
		- - T - -	(SEQ ID NO. 201)
		- - T - -	(SEQ ID NO. 202)
		- - T - ACT 3'(1839)	(SEQ ID NO. 203)
B	(2284) 5'	GGC GGC GGC TCT	(SEQ ID NO. 204)
		- GGT GGT GGT -	(SEQ ID NO. 205)
		- - GGC GGC -	(SEQ ID NO. 206)
		GAG - - GGC -	(SEQ ID NO. 207)
		- - - GGT -	(SEQ ID NO. 208)
		- - - GGC -	(SEQ ID NO. 209)
		- - - GGT -	(SEQ ID NO. 210)
		- - - GGC - 3'(2379)	(SEQ ID NO. 211)
Reverse complement of mutagenic oligo G3Bamlink			
	5'	GAG GGT GGC GGA TCC	(SEQ ID NO. 212)
		GAG GGT GGC GG 3'	(SEQ ID NO. 213)

Fig.17.

1) PRIMARY PCR



2) ASSEMBLY PCR



3) ADDING RESTRICTION SITES

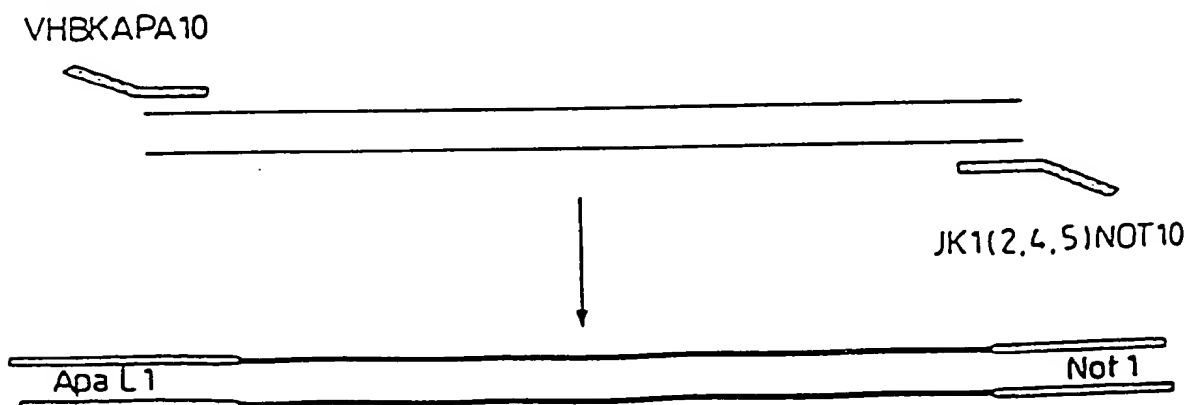


Fig.18.

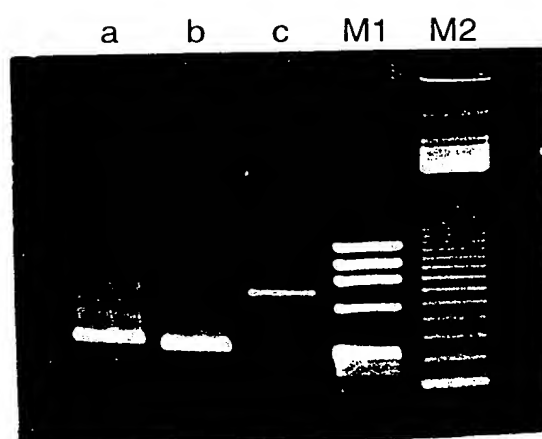


Fig.19.

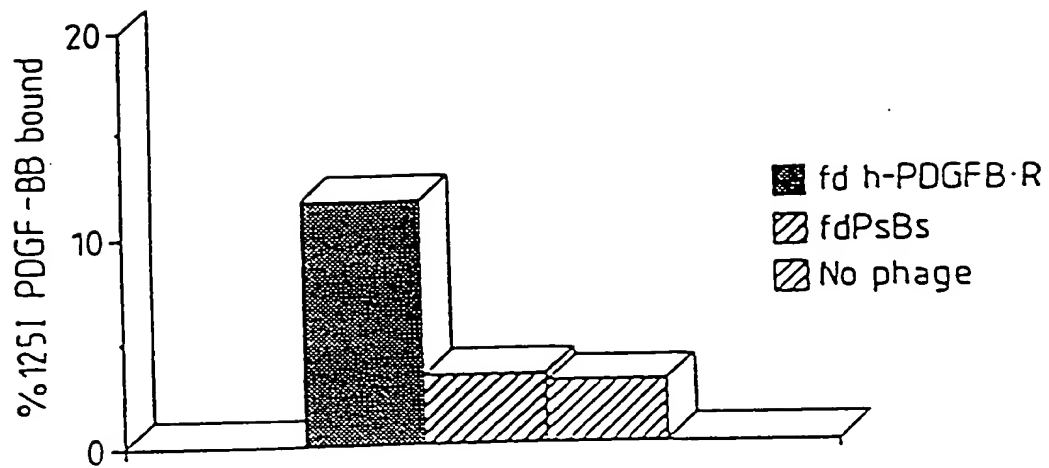


Fig.20.

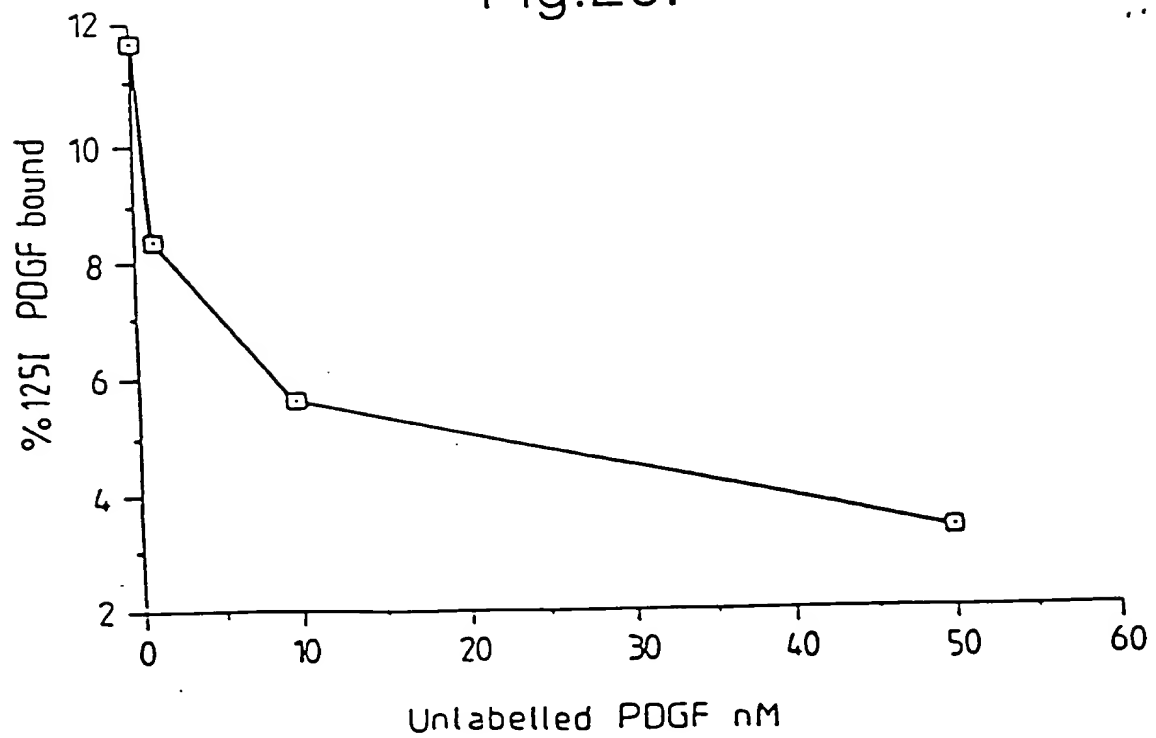


Fig.21.

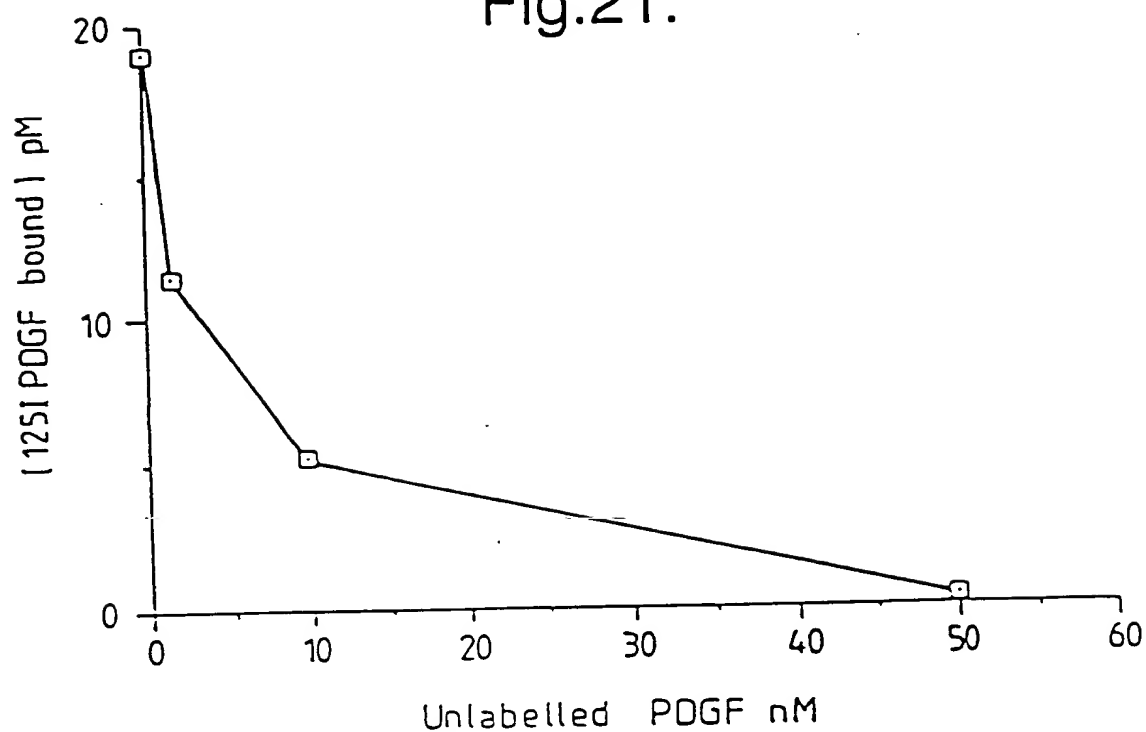


Fig.22.

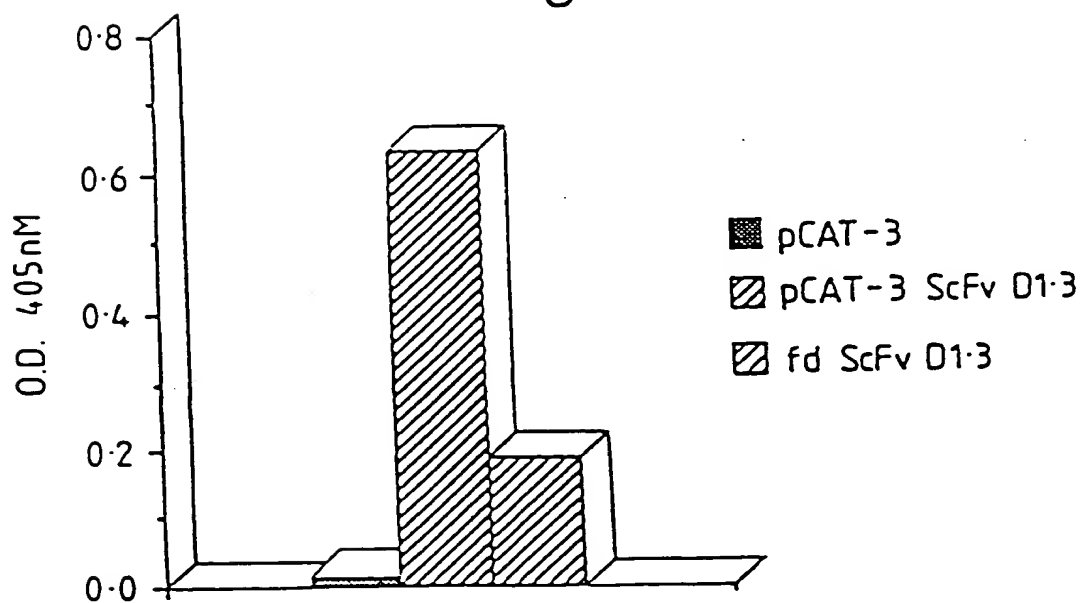


Fig. 23a

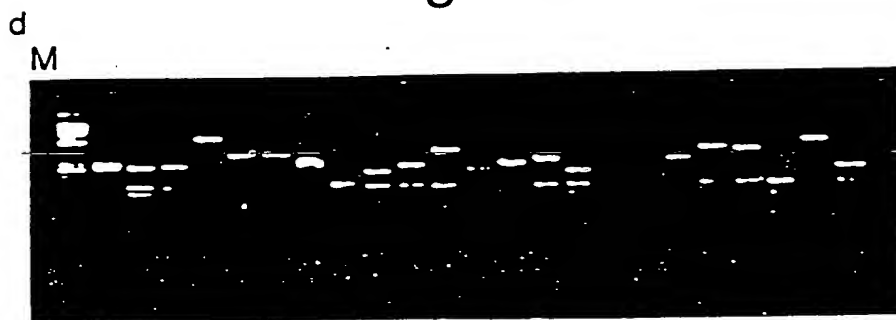


Fig. 23b

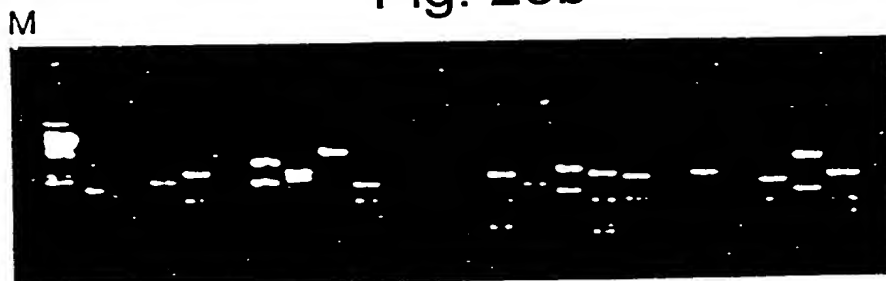


Fig. 24a

VH sequences

from combinatorial library:

		CDR1		CDR2		CDR3		
A	QVQLQQS0AELARPGASVXHSCKASGTTT	STTHI	WVKQRPQCGLEWIG	YINPSCGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	RYGAY	WQGTITVTVS9	x4 (SEQ ID NO. 214)
B	QVQLQQS0AELAKPGAEVXHSCKASGTTT	RDTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	NYGLY	WQGTITVTVS9	x9 (SEQ ID NO. 215)
C	QVQLQQSGPELVKPGAEVXHSCKASGTTT	SYTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	YRSPFY	WQGTITVTVS9	x3 (SEQ ID NO. 216)
D	QVQLQQSGPELVKPGAEVXHSCKASGTTT	GYTHI	WVKQRPQCGLEWIG	RIHPYHODTFYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	ITTRFAY	WQGTITVTVS9	x3 (SEQ ID NO. 217)
E	QVQLQQSGPELVKPGAEVXHSCKASGTTT	SYTHI	WVKQRPQCGLEWIG	VIWAGSTYTHQKFKD	RLSISKHSKSVFLKRISSLTQDDTAHYTCAR	URGDY	WQGTITVTVS9	2 V10x1 (SEQ ID NO. 218)
F	QVQLQQSGPELVKPGAEVXHSCKASGTTT	SYTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	1 (SEQ ID NO. 219)
G	QVQLQQS0AELVRLPGAEVXHSCKASGTTT	RTTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	ENTLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	1 (SEQ ID NO. 220)
H	QVQLQQSGPELVKPGAEVXHSCKASGTTT	RTTHI	WVKQRPQCGLEWIG	YIAPFNGCTTYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGRD	WQGTITVTVS9	1 (SEQ ID NO. 221)

from hierarchical library VH.rep x Vc-d:

I	QVQLQQSGPELVKPGAEVXHSCKASGTTT	STTHI	WVKQRPQCGLEWIG	VIETNGHTYTHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	1 (SEQ ID NO. 222)
J	QVQLQQSGPELVKPGAEVXHSCKASGTTT	RTTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DRGAY	WQGTITVTVS9	1 (SEQ ID NO. 223)
K	QVQLQQSGPELVKPGAEVXHSCKASGTTT	RDTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	NYGLY	WQGTITVTVS9	1 (SEQ ID NO. 224)
L	QVQLQQSGPELVKPGAEVXHSCKASGTTT	NYTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	x3 (SEQ ID NO. 225)
M	QVQLQQSGPELVKPGAEVXHSCKASGTTT	NYTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	x3 (SEQ ID NO. 226)
N	QVQLQQSGPELVKPGAEVXHSCKASGTTT	STTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	1 (SEQ ID NO. 227)
O	QVQLQQSGPELVKPGAEVXHSCKASGTTT	STTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	1 (SEQ ID NO. 228)
P	QVQLQQSGPELVKPGAEVXHSCKASGTTT	STTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	1 (SEQ ID NO. 229)
Q	QVQLQQSGPELVKPGAEVXHSCKASGTTT	STTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	1 (SEQ ID NO. 230)
R	QVQLQQSGPELVKPGAEVXHSCKASGTTT	STTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	1 (SEQ ID NO. 231)
S	QVQLQQSGPELVKPGAEVXHSCKASGTTT	STTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	1 (SEQ ID NO. 232)
T	QVQLQQSGPELVKPGAEVXHSCKASGTTT	STTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	x3 (SEQ ID NO. 233)
U	QVQLQQSGPELVKPGAEVXHSCKASGTTT	STTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	x6 (SEQ ID NO. 234)
V	QVQLQQSGPELVKPGAEVXHSCKASGTTT	RDTHI	WVKQRPQCGLEWIG	YINPSTGYTEYHQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	WQGTITVTVS9	1 (SEQ ID NO. 235)

Fig. 24b

V_k sequences

from combinatorial library:

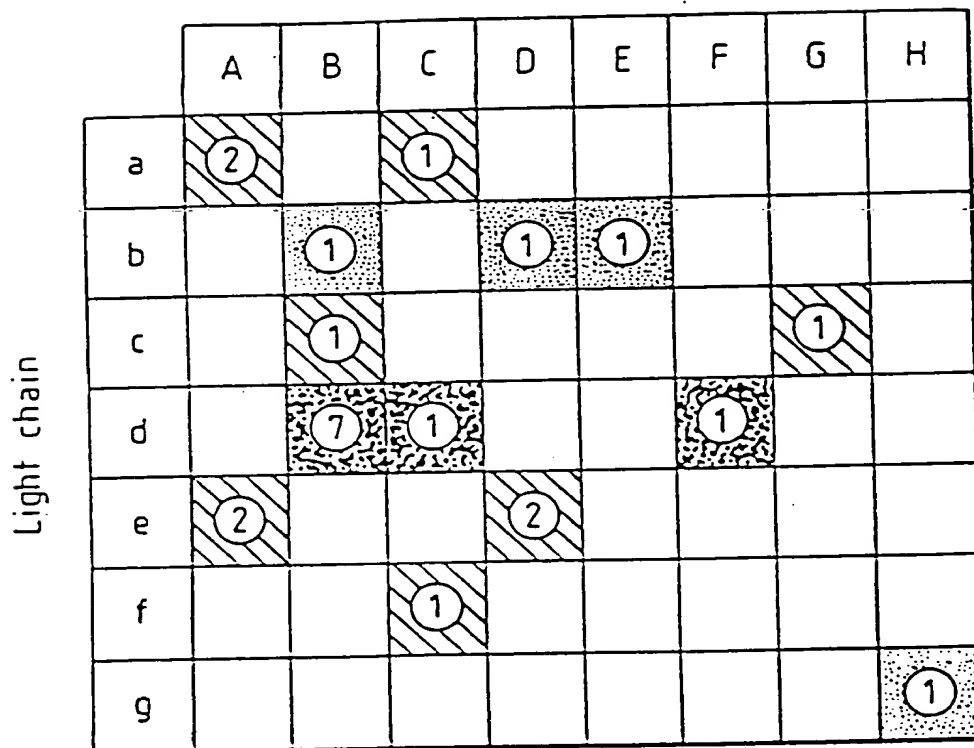
	CDR1	CDR2	CDR3		
a	DIELTQSPSSLSASLGERVLTTC	RAEQEISCTLS	WLOQKPGCSIRKLIIY	AASTLES	GVPAKFSGSGSGCTSYSLTISSEEDFADYYC
b	DIELTQSPAIHNSAPGERVNTTC	RASSSV66SYLH	WYQKSGASPKRMIIY	BTSHLAS	GVPAKFSGSGSGCTSYSLTISSEVEDAATYYC
c	DIELTQSPPTTHAASPGCKITITC	SASSS16SNTLH	WYQKPGFSPKLLIIY	RTSHLAS	GVPAKFSGSGSGCTSYSLTICTHAEADVATYYC
d	DIELTQSPPTTHAASPGCKITITC	SASSS16SNTLH	WYQKPGFSPKLLIIY	RTSHLAS	GVPAKFSGSGSGCTSYSLTICTHAEADVATYYC
e	DIELTQSPAIHNSAPGERVNTTC	SASSSVNTDII	WYQKPGCTSPKLMIIY	STSHLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC
f	DIELTQSPALHSAFPGCKVHTTC	SAS9SV5YTH	WYQKSGTSPKRMIIY	DTSKLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC
g	DIELTQSPAIHNSAPGERVNTTC	SASSSINTDII	WYQKPGASPKRMIIY	DTSKLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC

from hierarchical library VII-B x Ve-rep:

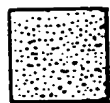
h	DIELTQSPAIHNSAPGERVNTTC	SASSSV5TDII	WYQKSGTSPKRMIIY	DTSKLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC	QOM6SIPPLT	FGAGTKLEIKRA	x3	IV/V1	Vkox1	(SEQ ID NO. 243)
i	DIELTQSPAIHNSAPGERVNTTC	SASSSV6TIIH	WYQKPGCTSPKLMIIY	STSHLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC	QOM5IPPLT	FGAGTKLEIKRA	x3	V	ox-1ike?	(SEQ ID NO. 244)
j	DIELTQSPPTTHAASPGCKITITC	SASSS15SNTLH	WYQKPGFSPKLLIIY	RTSHLAS	GVPAKFSGSGSGCTSYSLTICTHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	V	ox-1ike	(SEQ ID NO. 245)
k	DIELTQSPPTTHAASPGCKITITC	SATS61SSNTLH	WYQKPGFSPKLLIIY	RTSHLAS	GVPAKFSGSGSGCTSYSLTICTHAEADVATYYC	QOM6SIPPLT	FGAGTKLEIKRA	x3	V	ox-1ike	(SEQ ID NO. 246)
l	DIELTQSPPTTHAASPGCKITITC	SASSS15SNTLH	WYQKPGFSPKLLIIY	RTSHLAS	GVPAKFSGSGSGCTSYSLTICTHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	V	ox-1ike	(SEQ ID NO. 247)
m	DIELTQSPPTTHAASPGCKITITC	SASSS15SNTLH	WYQKPGFSPKLLIIY	RTSHLAS	GVPAKFSGSGSGCTSYSLTICTHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	V	ox-1ike	(SEQ ID NO. 248)
n	DIELTQSPPTTHAASPGCKITITC	SASSS15SNTLH	WYQKPGFSPKLLIIY	RTSHLAS	GVPAKFSGSGSGCTSYSLTICTHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	V	ox-1ike	(SEQ ID NO. 249)
o	DIELTQSPAIHNSAPGERVNTTC	SASSS15SNTLH	WYQKPGCTSPKRMIIY	DTSKLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	V	ox-1ike	(SEQ ID NO. 250)
p	DIELTQSPAIHNSAPGERVNTTC	SASSSV5TDII	WYQKPGCTSPKRMIIY	DTSKLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	IV/V1	Vkox1	(SEQ ID NO. 251)
q	DIELTQSPAIHNSAPGERVNTTC	SASSSVNTVN	WYQKPGCTSPKRMIIY	DTSKLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	IV/V1	Vkox1	(SEQ ID NO. 252)
r	DIELTQSPAIHNSAPGERVNTTC	SASSSV6TDII	WYQKPGCTSPKRMIIY	DTSKLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	IV/V1	Vkox1	(SEQ ID NO. 253)
s	DIELTQSPAIHNSAPGERVNTTC	RASSSV58YTH	WYQKPGASPKLMIIY	BTSHLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	IV/V1	ox-1ike	(SEQ ID NO. 254)
t	DIELTQSPAIHNSAPGERVNTTC	RASSSV96SYLH	WYQKPGASPKLMIIY	BTSHLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	IV/V1	ox-1ike	(SEQ ID NO. 255)
u	DIELTQSPAIHNSAPGERVNTTC	RASSSV56SYLH	WYQKPGASPKLMIIY	BTSHLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	IV/V1	ox-1ike	(SEQ ID NO. 256)
v	DIELTQSPAIHNSAPGERVNTTC	RASSSV56SYLH	WYQKPGASPKLMIIY	BTSHLAS	GVPAKFSGSGSGCTSYSLTISSEHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	IV/V1	ox-1ike	(SEQ ID NO. 257)
w	DIELTQSPPTTHAASPGCKITITC	SASSS15SNTLH	WYQKPGFSPKLLIIY	RTSHLAS	GVPAKFSGSGSGCTSYSLTICTHAEADVATYYC	QOM5SIPPLT	FGAGTKLEIKRA	x3	IV/V1	ox-1ike	(SEQ ID NO. 258)

Fig.25.

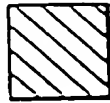
HEAVY CHAIN



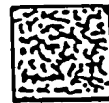
OD_{405nm} in ELISA



0.2-0.9



0.9-2.0



>2.0

Fig.26(a).

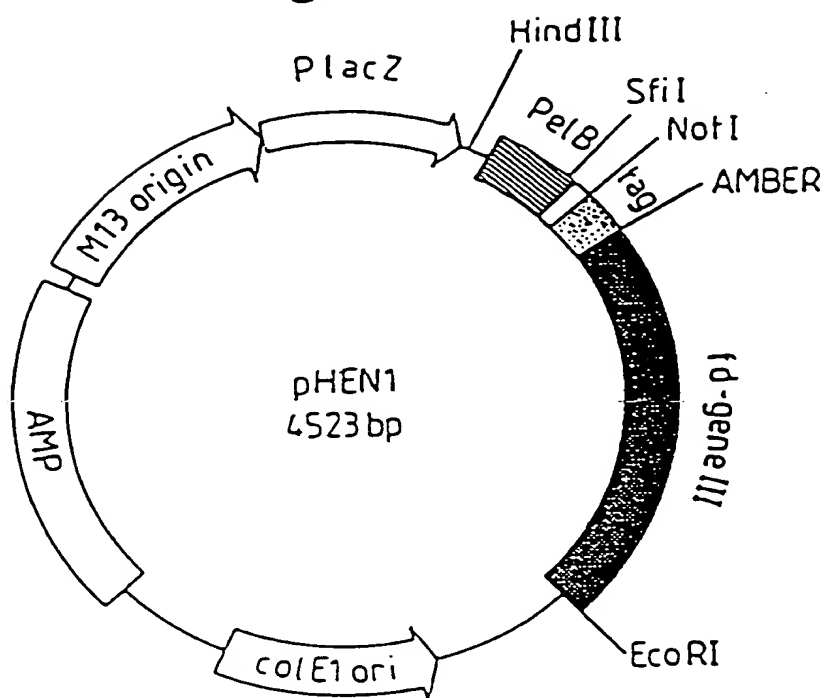


Fig.26(b).

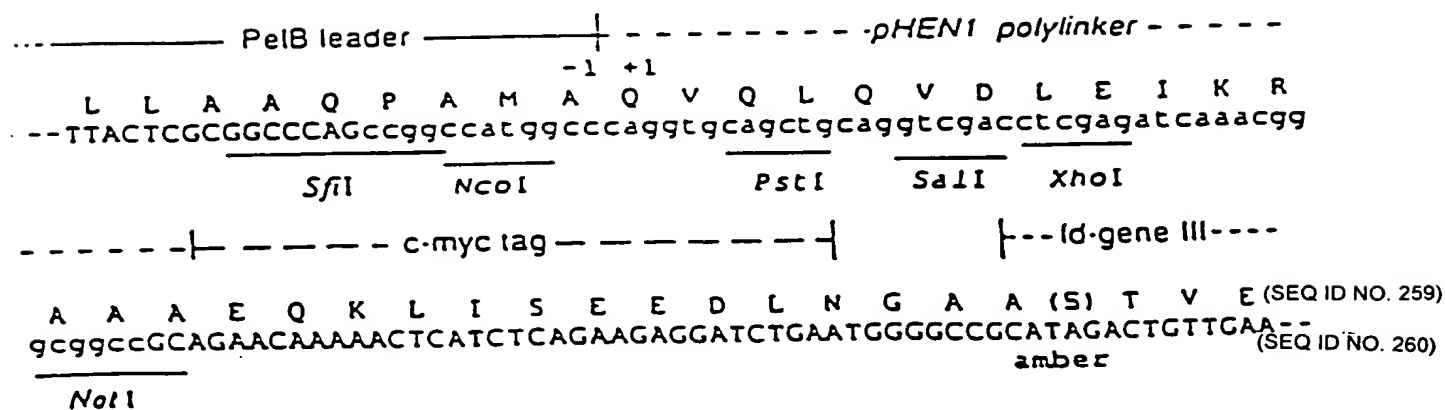


Fig.27.

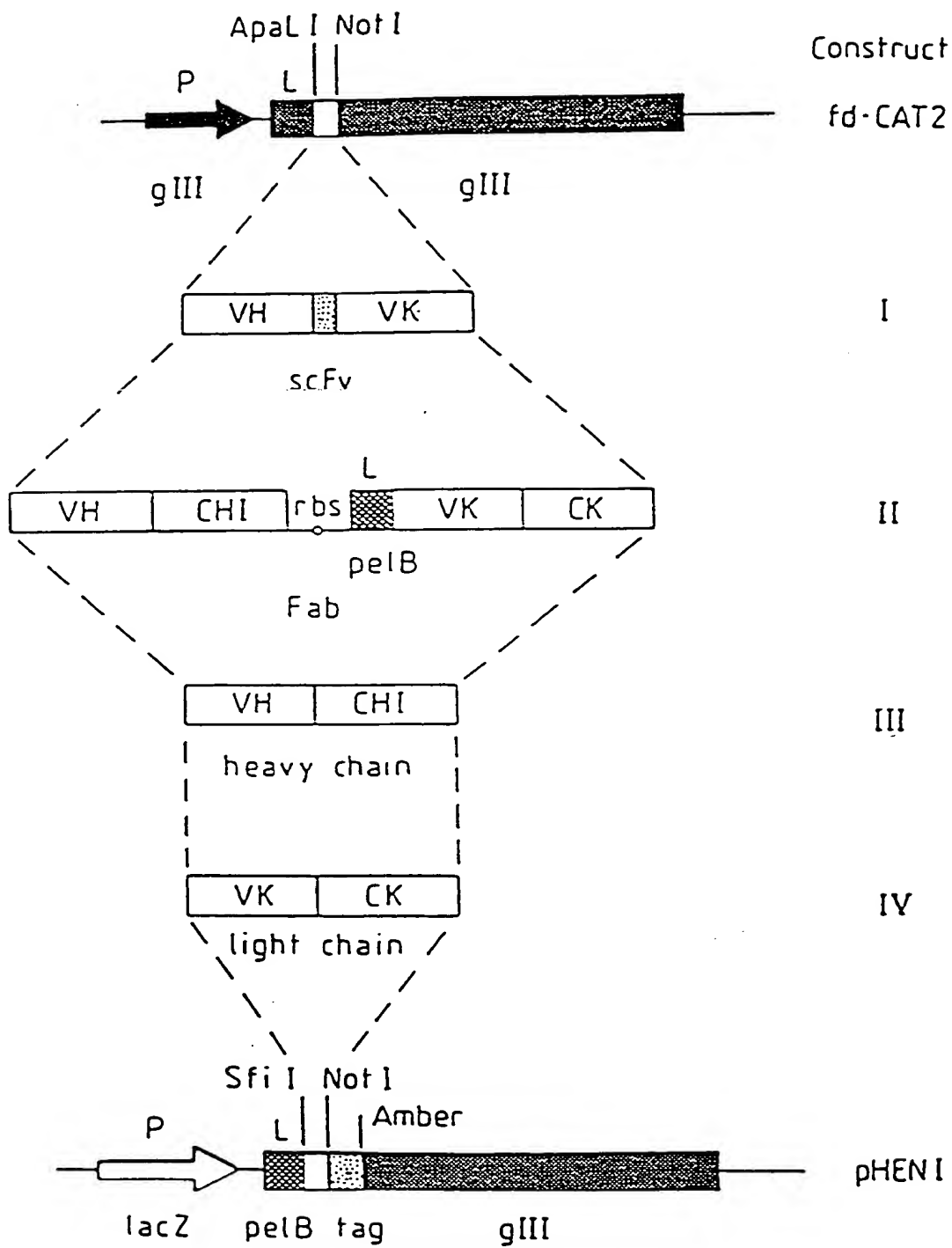


Fig.28.

Fab

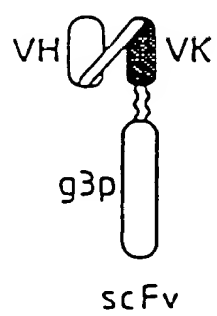
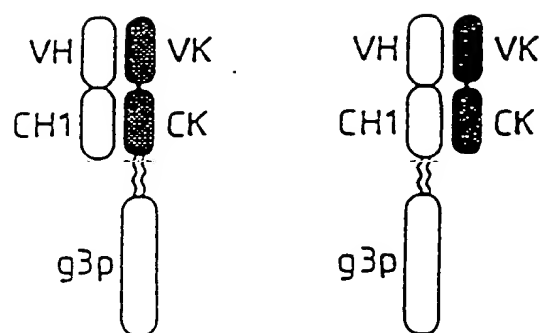


Fig.29.

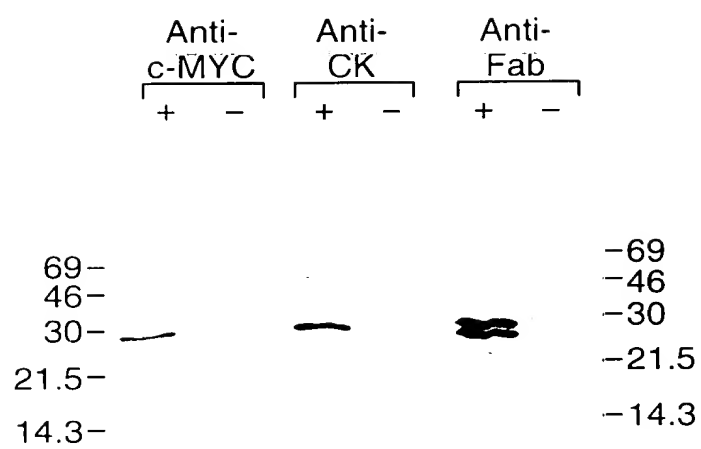


Fig.30.

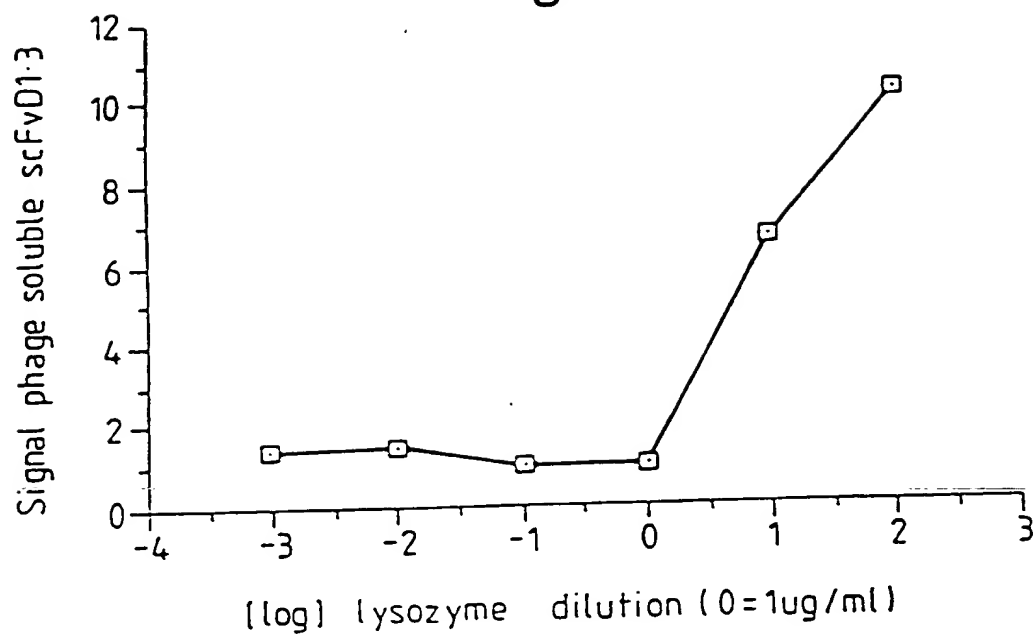


Fig.31.

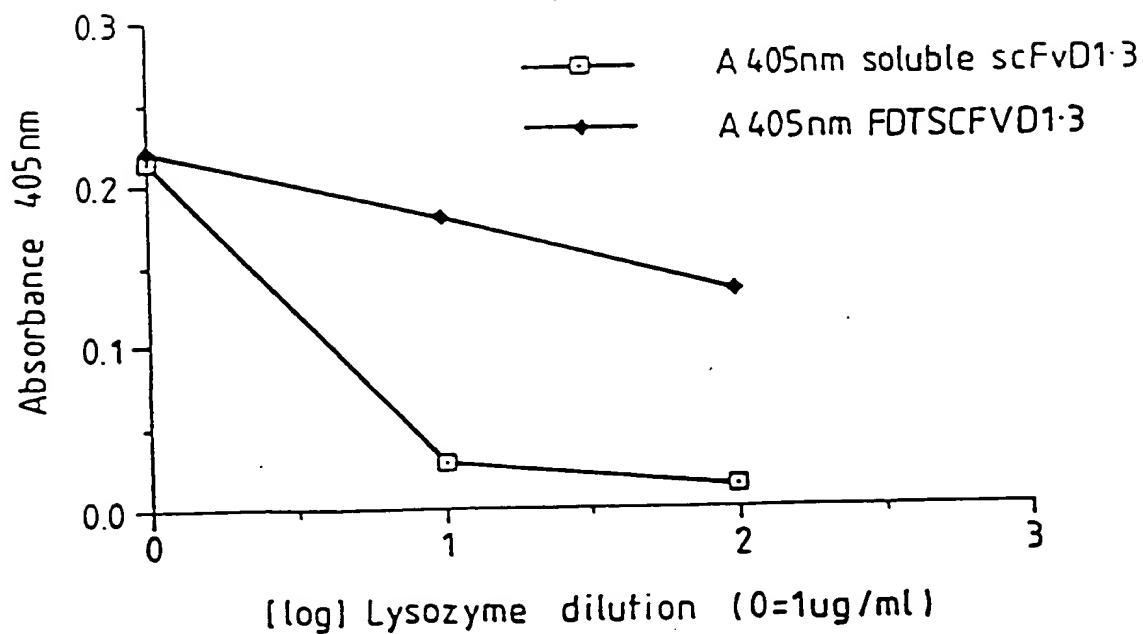


Fig.32.

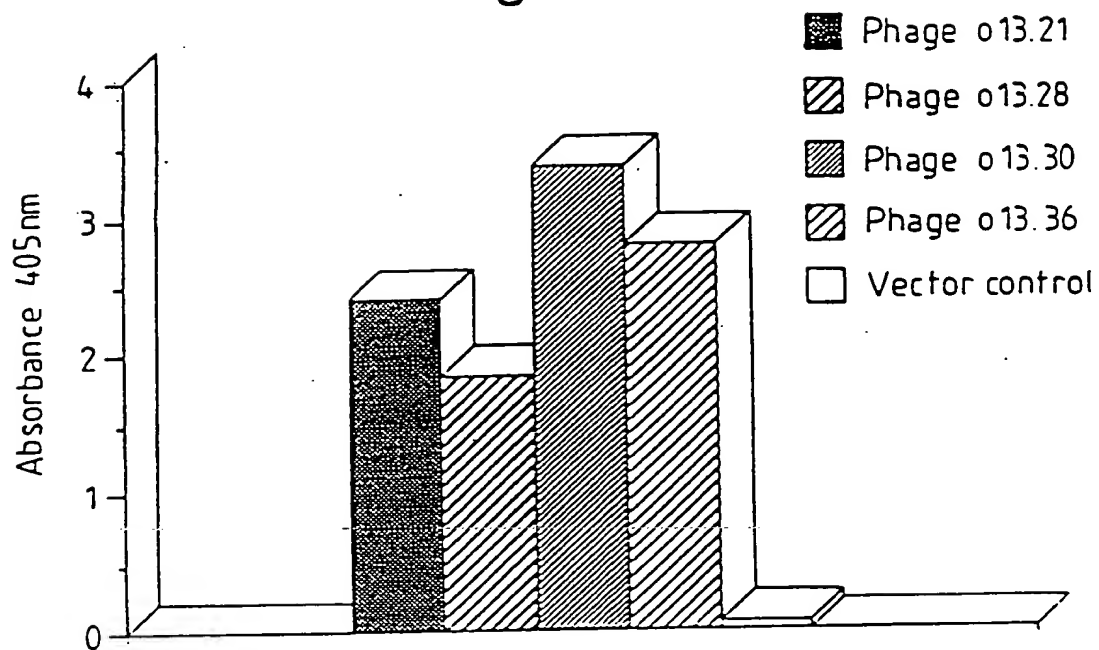


Fig.33.

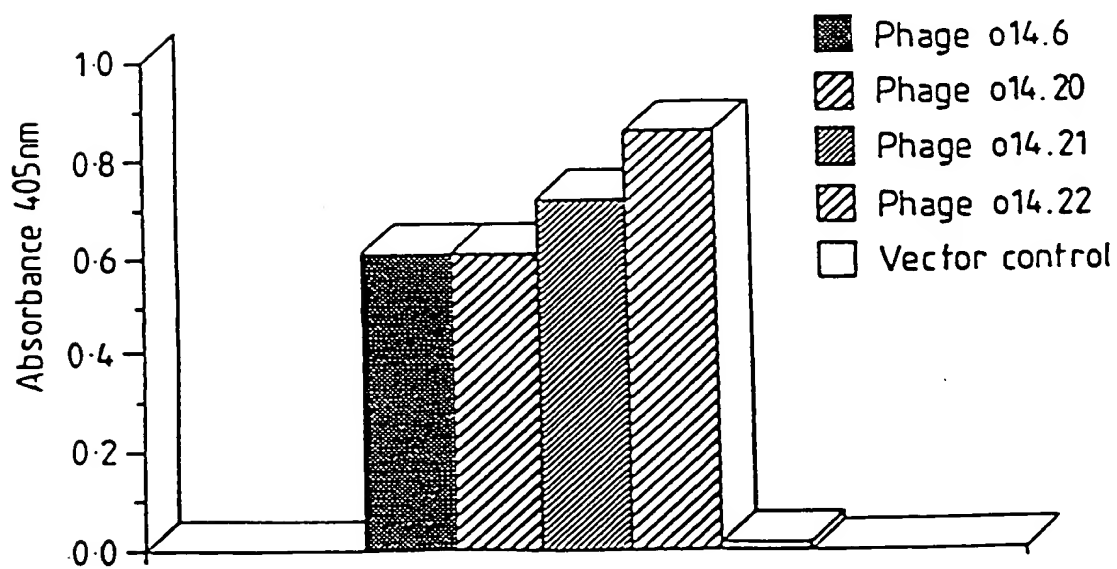


Fig.34.

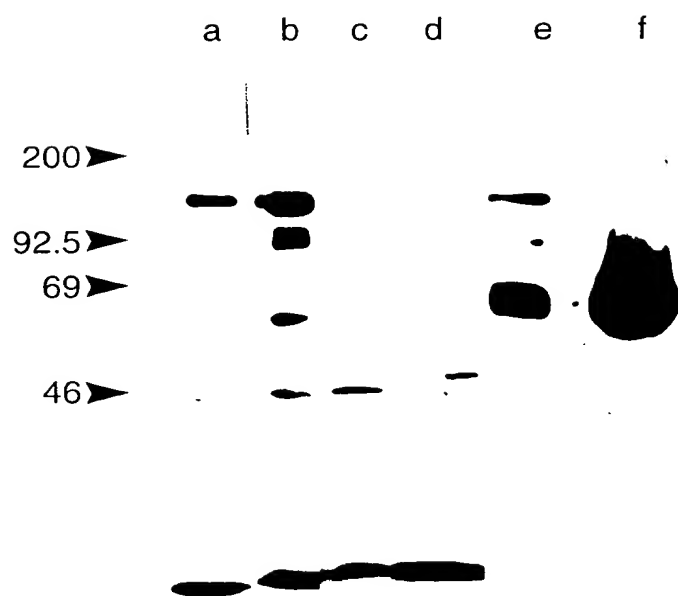


Fig.35A.

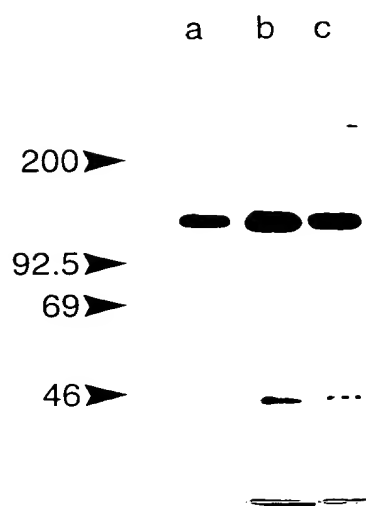


Fig.35B.

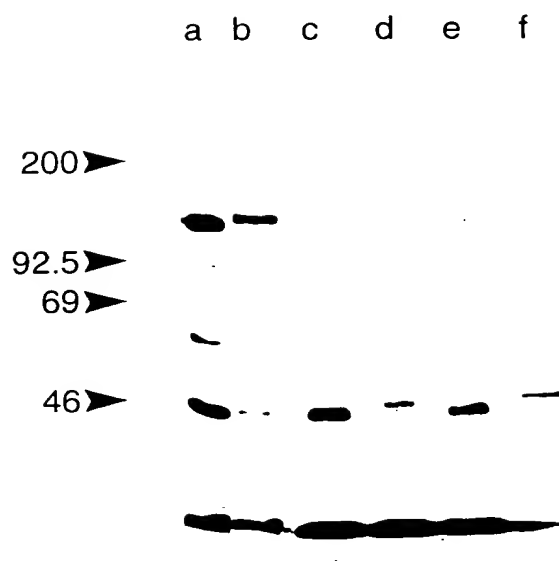


Fig.36.

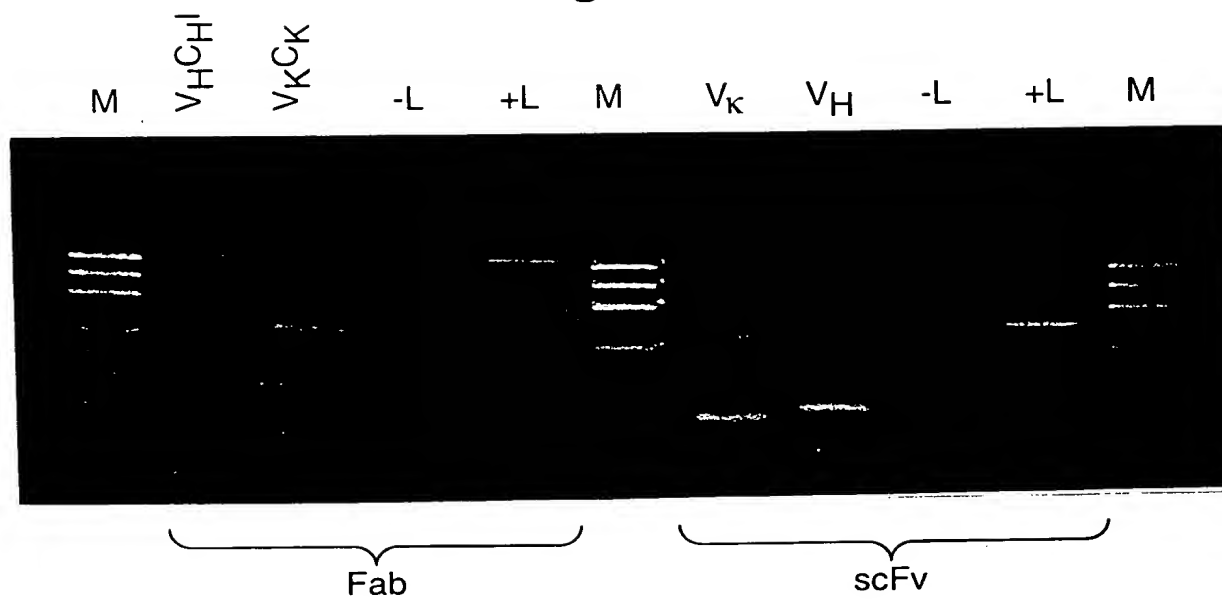


Fig.37.

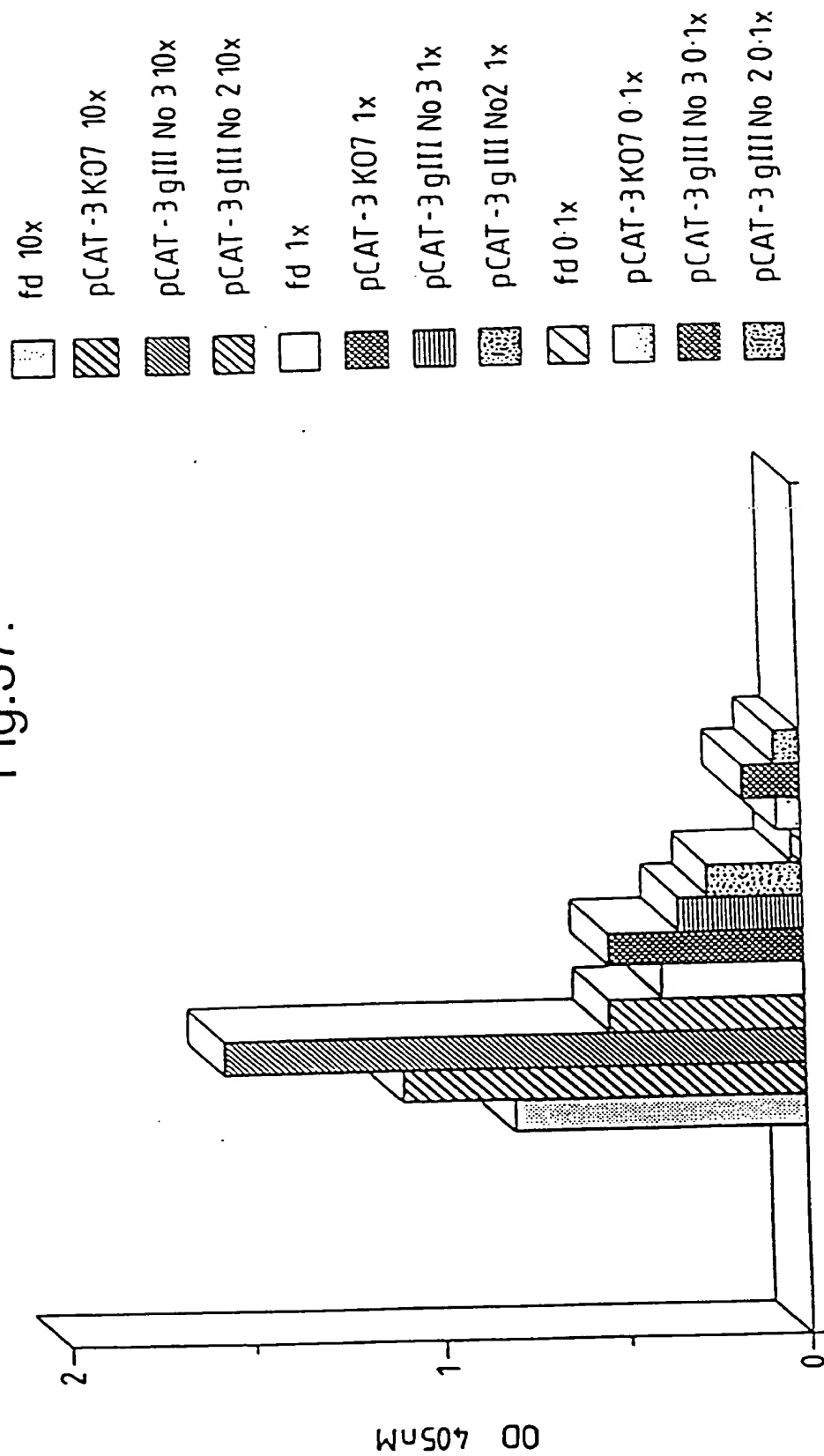


Fig.38A.

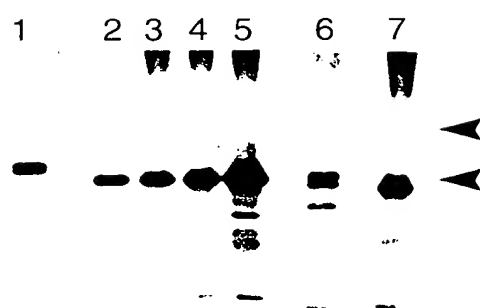


Fig.38B.

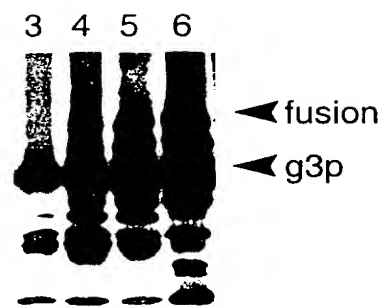


Fig.39.

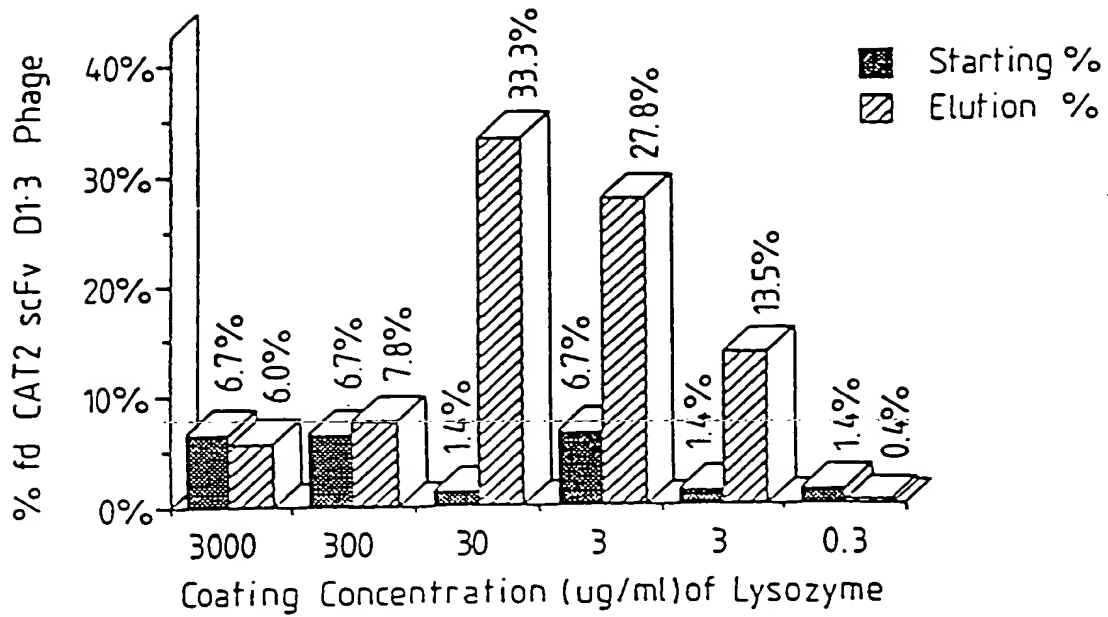


Fig.40.

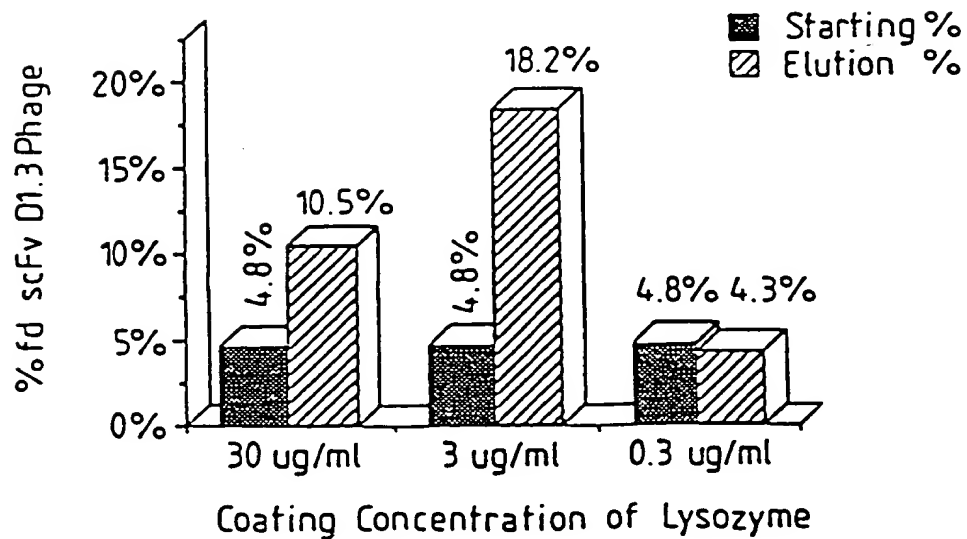


Fig.41.

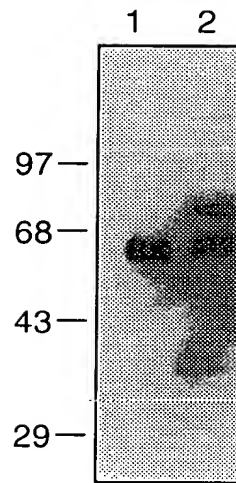


Fig.42.

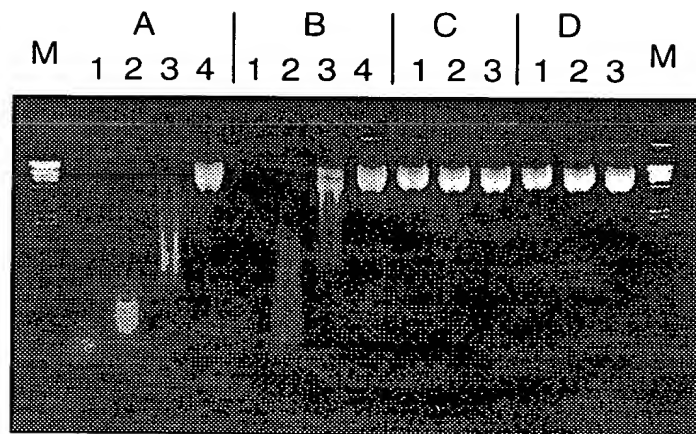


Fig.43.

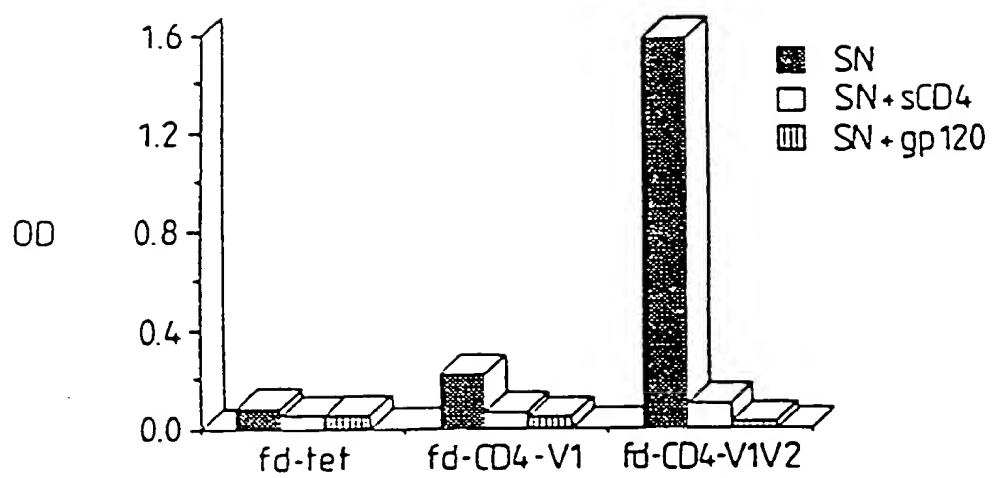


Fig. 44a

10 20 30 40 50 60 70 80 90
 TTCTATTCTCACNGTGCNCAGGTCCAGCTGCAGCAGTCTGGGGCTGAGCTTGTGNAAGCCTGGGGCTTCAGTGAGCTGTCTCTGCAAGGCT
 AAGATAAGAGTGTACGTTGTCCAGGTTCGACGTCGTTCAGACCCCGACTTCGACACTTCGGACCCCGAAGTCACCTTCGACAGGACGTTCCGA
 PheTyrSerHisSerAlaGlnValGlnLeuGlnSerGlyAlaGluLeuValLysProGlyAlaSerValLysLeuSerCysLysAla
 100 110 120 130 140 150 160 170 180
 TCTGGCTACACCTTCACACGCTACTGGATGCNCTGGGTGANGCAGAGGCCCTGGACGAGGCCCTTGAGTGGATTGGNAGGATTGATCCTAAT
 AGACCGATGTGGNAGTGGTCGATGACCTACGTGACCCACTTCGTCTCCGGACCTGCTCCGGNACTCACCTAACCTTCTCCTAAGGATT
 SerGlyTyrThrPheThrSerTyrTrpMetHisTrpValLysGlnArgProGlyArgGlyLeuGluTrpIleGlyArgIleAspProAsn
 190 200 210 220 230 240 250 260 270
 AGTGGTGGTACTAAGTACNATGAGNAGTTCAAGAGCMAAGGCCACACTGACTGTAGACAAACCCCTCCAGCACAGCCTACATGCAGCTCAGC
 TCACCAACCATGATTCTTACTCTTCAAGTTCTCGTTCGGGTGACTGACATCTGTTTGGAGGTCGTGTCGGATGTACGTTCGAGTCG
 SerGlyGlyThrLysTyrAsnGluLysPheLysSerLysAlaThrLeuThrValAspLysProSerSerThrAlaTyrMetGlnLeuSer
 280 290 300 310 320 330 340 350 360
 AGCCTGACATCTGAGGACTCTGCGGTCTATTATTGTGCAAGNTACGACTACGGTAGTAGCTACTACTTTGACTACTGGGGCCAAAGGGACC
 TCGGACTGTAGACTCCTGAGACGCCAGATAATAACACGTTCTATGCTGATGCCATCATCGATGATGMACTGATGACCCCGTTCCTCCG
 SerLeuThrSerGluAspSerAlaValTyrTyrCysAlaArgTyrAspTyrGlySerSerTyrTyrPheAspTyrTrpGlyGlnGlyThr
 370 380 390 400 410 420 430 440 450
 ACGGTACCCGTCTCCTCNGGTGGAGGCGGTTTCAGGGCGGAGGTGGCTCTGGCGGTGGCGGATCCCGGCTGGGGACACAGGMAATCTGCA
 TGCCAGTGGCAGAGGATCCACCTCCGCCCTCCACCGAGACCGCCACCGCTAGGGTCCGACAAACCCCTGTCTCTTAGACGT
 ThrValThrValSerSerGlyGlyGlySerGlyGlyGlySerGlyGlyGlySerGlnAlaValGlyThrGlnGluSerAla
 460 470 480 490 500 510 520 530 540
 CTCACACATCACCTGGTGAACAGATCACACTACTTGTGCTCAGTACTGGGGCTGTTACAACTAGTAACTATGCCAACTGGGTCCAA
 GAGTGGTGTAGTGGACCACTTTGTCAAGTGTGAGTGAACAGCGAGTTTCATGACCCCGACAAATGTTGATCATTTGATACGTTGACCCAGGTT
 LeuThrThrSerProGlyGluThrValThrLeuThrCysArgSerSerThrGlyAlaValThrThrSerAsnTyrAlaAsnTrpValGln
 550 560 570 580 590 600 610 620 630
 GAAACACAGATCATTTATTCACTGGTCTAATAGGTGGTACCAACAAACCGAGCTCCAGGTGTTCTCGCCAGATTCTCAGGCTCCCTGATT
 CTTT'TGGTCTAGTAAATAAGTGACCAAGATTATCCACCATGTTGTTGGCTCGAGGTCCACAAAGGACGGTCTAAGAGTCCGAGGACCTAA
 GluLysProAspHisLeuPheThrGlyLeuIleGlyGlyThrAsnAsnArgAlaProGlyValProAlaArgPheSerGlySerLeuIle

Fig. 44b

640 650 660 670 680 690 700 710 720
 GGAGACAAGGCTGCCCTCACCATCACAGGGGCGCACAGACTGAGGNTGAGGCCAATATATTTCTGTGCTCTATGCTACAGCAACCATTTGGGTG
 CCTCTGTTCCGACGGGAGTGTAAGTGTCCCGTGTCTGACTCCTACTCCGTTATATAAGACACAGAGATACCATGCTCGTTGGTAACCCAC
 GlyAspLysAlaAlaLeuThrIleThrGlyAlaGlnThrGluAspGluAlaIleTyrPheCysAlaLeuTrpTyrnberAsnHisTrpVal
 730 740 750 760 770
 TTCGTGGAGGAAACAAACTGACTGTCTCTCGAGATCAAAACGGCGCGCCGC (SEQ ID NO. 261)
 AAGCCACCTCCTTGTTGACTGACAGGAGCTCTAGTTTGCCCGCCGCGCG
 PheGlvGlyGlyThrLysLeuThrValLeuGluIleLysArgAlaAla (SEQ ID NO. 262)

Fig.45.

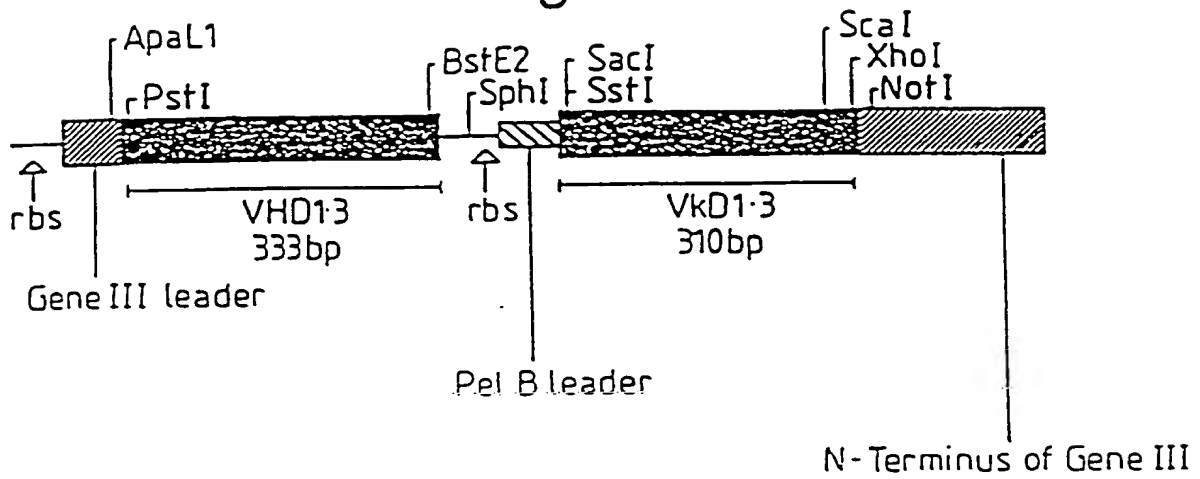


Fig.46.

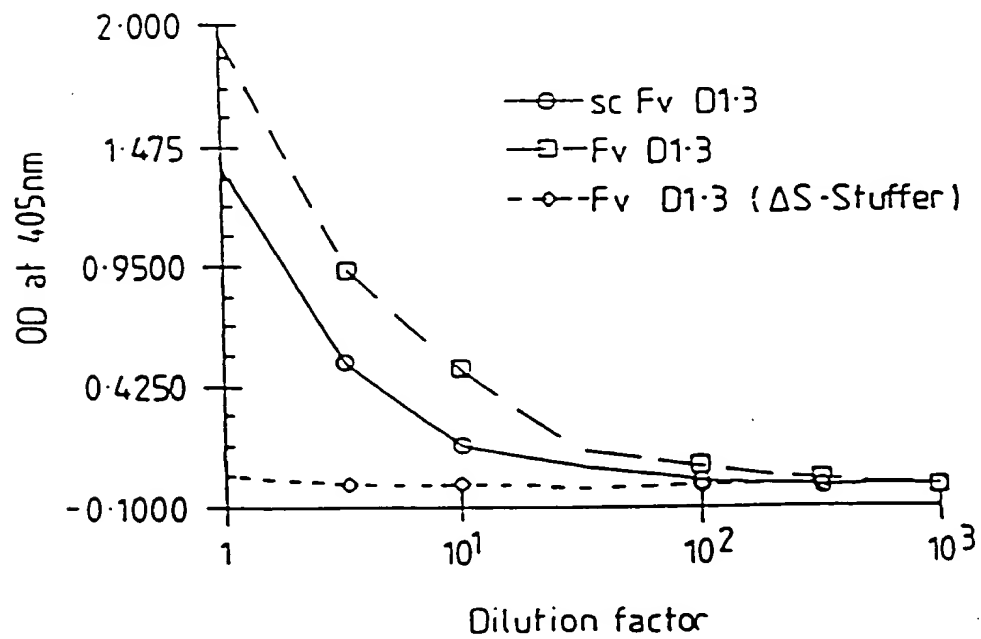


Fig.47.

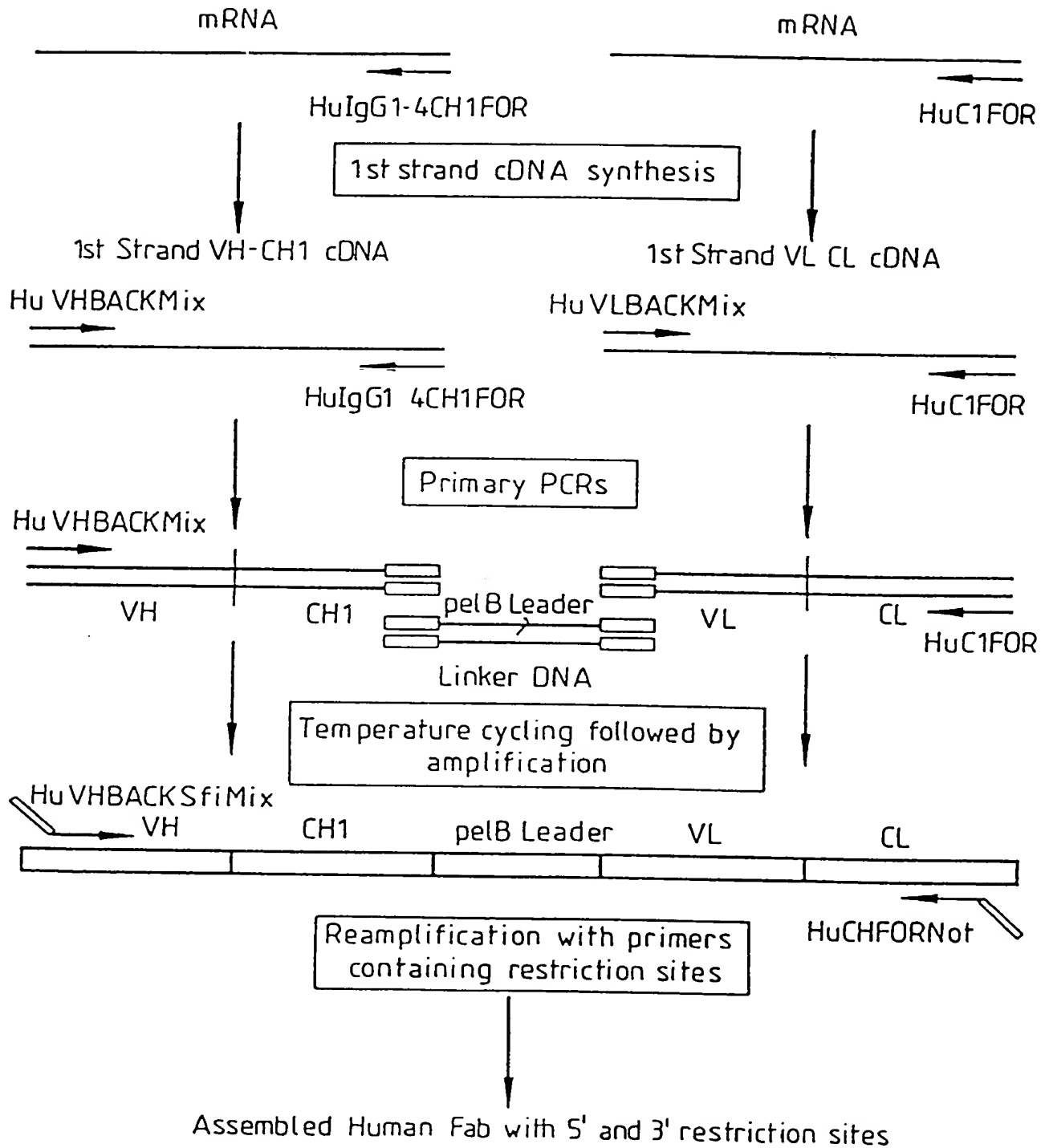


Fig. 48a

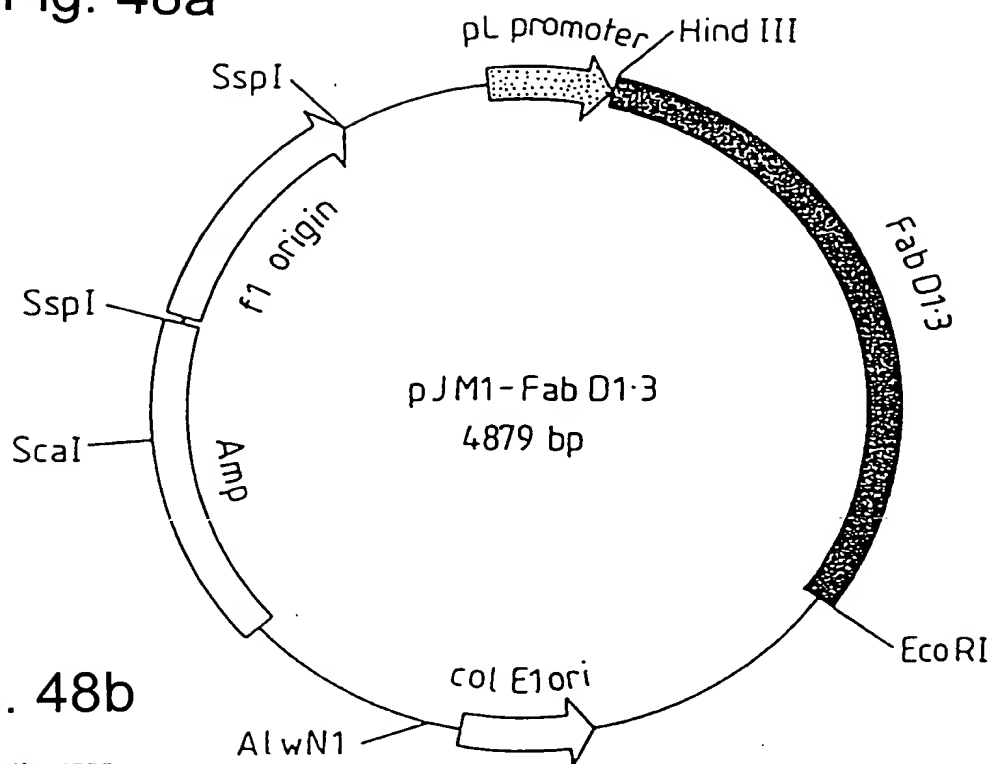


Fig. 48b

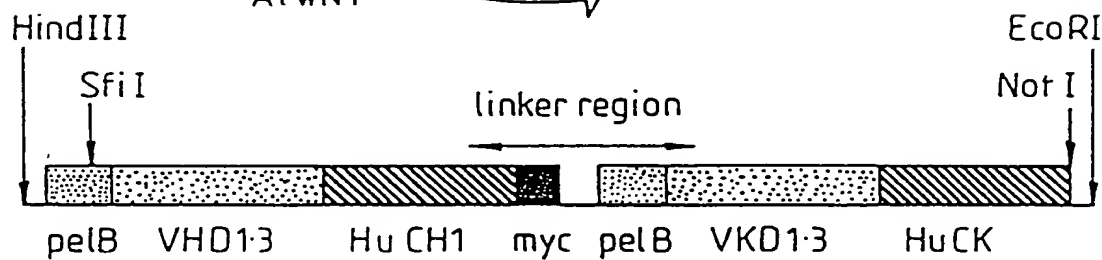


Fig. 48c

Sequence of linker region

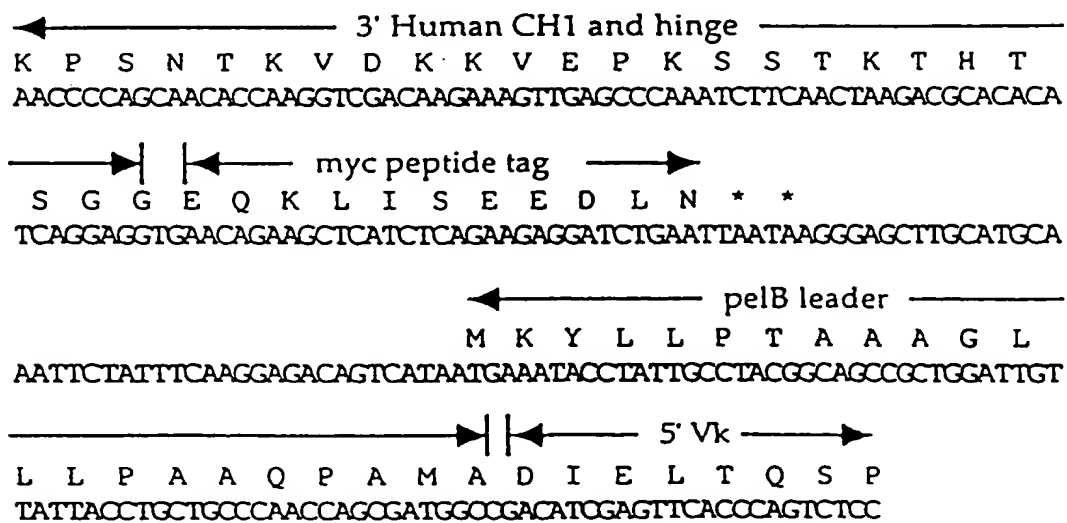


Fig.49.

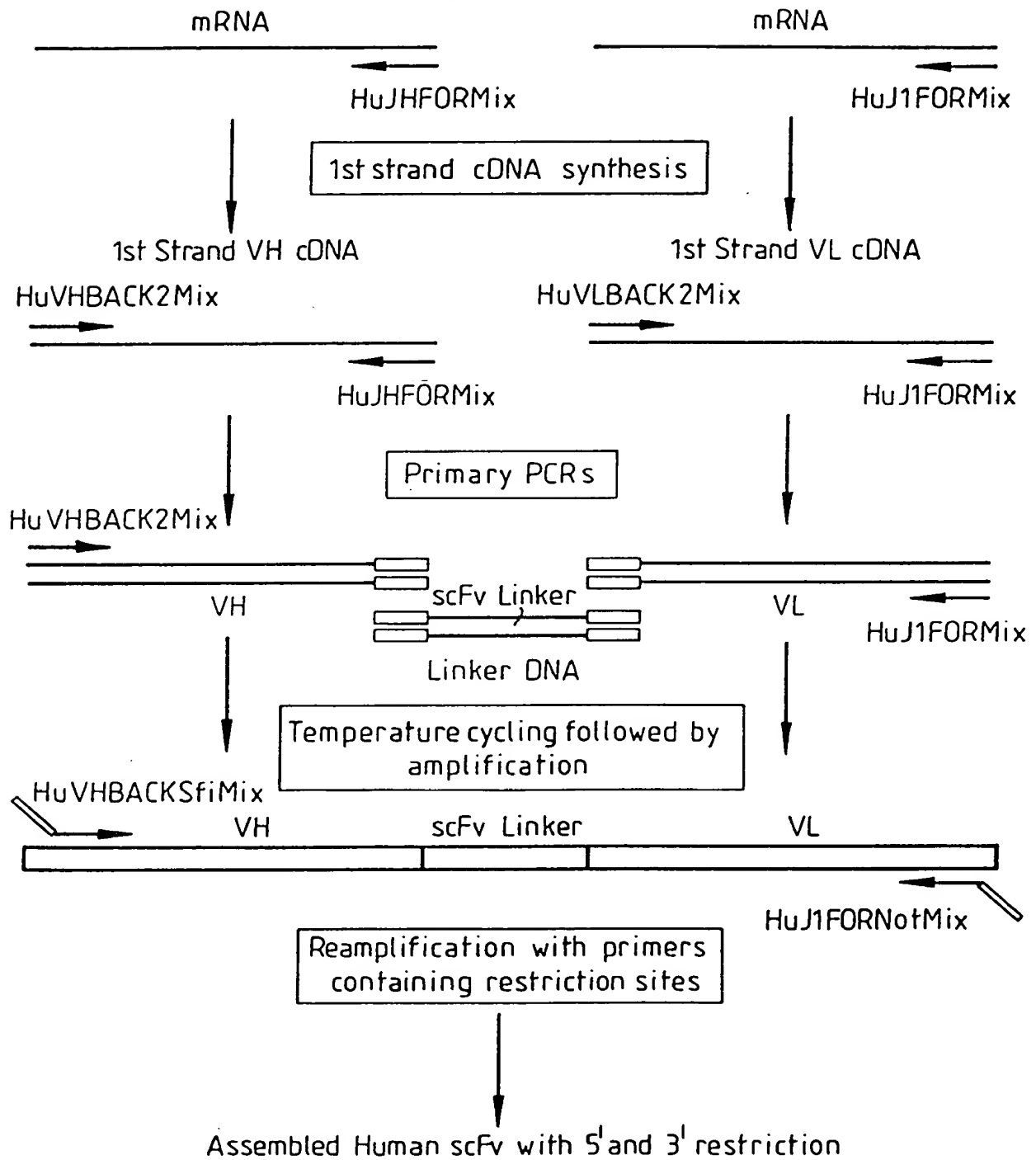


Fig. 50a

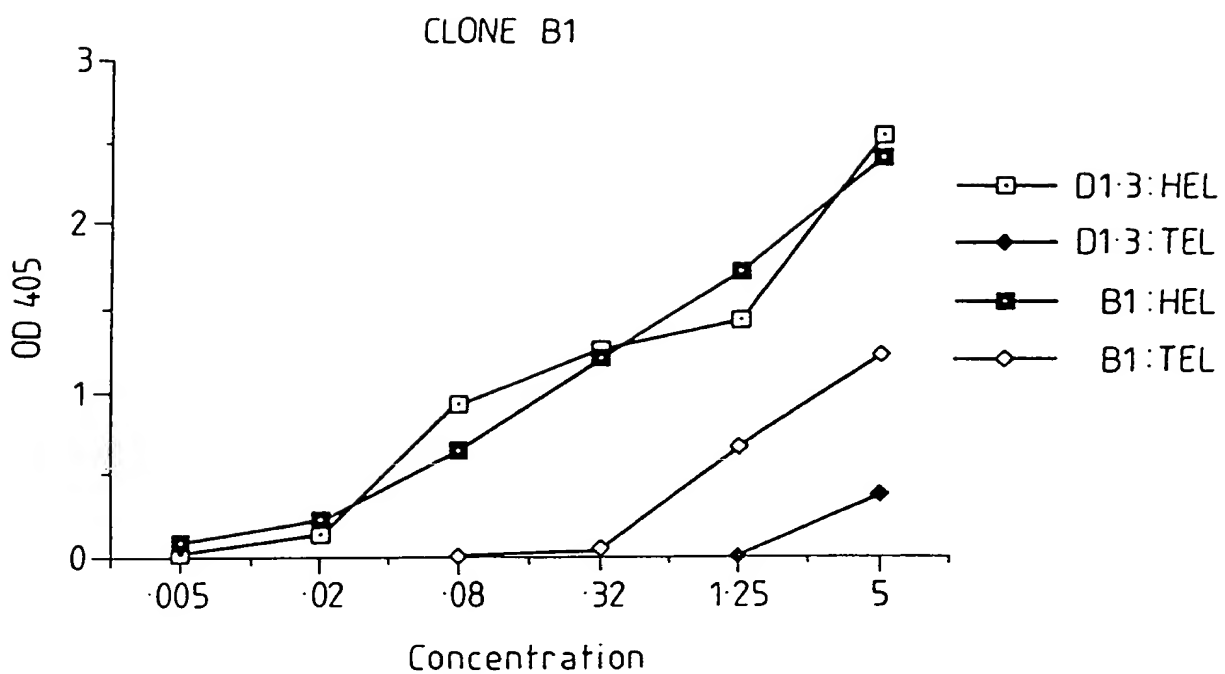


Fig. 50b

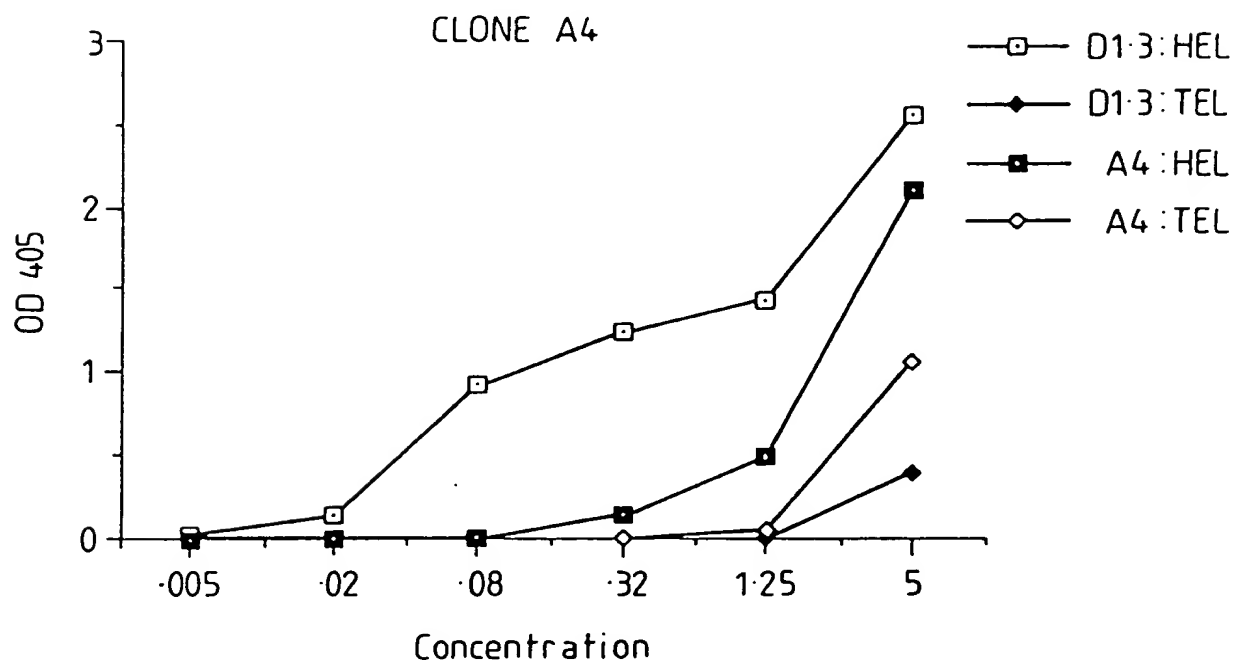


Fig.52.

CDR 1

CDR 2

D1.3 DIQMTQSPASLSASVGETVTITCRASGNIHNYLA WYQQKQKSPQLLVYTTTLAD
M1F DIELTQSPSSLSASLGERVSLTCRASQDIGSSLN WLQQEPDGTIKRRIYATSSLDS
M21 DIELTQSPALMAASPGEKVTITCSVSSSISSSNLHWYQQKSETSPKPWIYGTSNLAS

CDR 3

D1.3 GVPSRFGSGGTQYSLKINSLQPEDFGSYQCQHFWSPTPTFGGGTKLEIKR
M1F GVPKRFSGSRGSDYSLTISSESEDFVDYVCLQYASSPWTFGGGTKLELKR
M21 GVPVRFSGSGGTSYSLTISSEAEADAATYVCCQWSSYPVLTFGAGTKLEIKR

Fig.51.

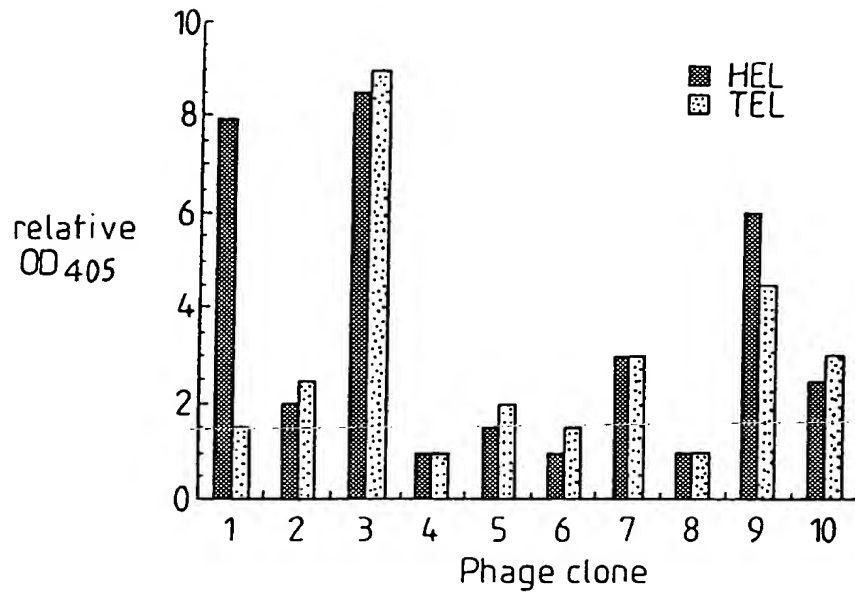


Fig.53.

